

2014

PHYSIOLOGICAL MODELS OF  
GEOBACTER SULFURREDUCTENS AND  
DESULFOBACTER POSTGATEI TO  
UNDERSTAND URANIUM REMEDIATION  
IN SUBSURFACE SYSTEMS

Roberto Orellana

*umass*, [orellana@microbio.umass.edu](mailto:orellana@microbio.umass.edu)

Follow this and additional works at: [http://scholarworks.umass.edu/dissertations\\_2](http://scholarworks.umass.edu/dissertations_2)

---

**Recommended Citation**

Orellana, Roberto, "PHYSIOLOGICAL MODELS OF GEOBACTER SULFURREDUCTENS AND DESULFOBACTER POSTGATEI TO UNDERSTAND URANIUM REMEDIATION IN SUBSURFACE SYSTEMS" (2014). *Doctoral Dissertations 2014-current*. Paper 278.

This Open Access Dissertation is brought to you for free and open access by the Dissertations and Theses at ScholarWorks@UMass Amherst. It has been accepted for inclusion in Doctoral Dissertations 2014-current by an authorized administrator of ScholarWorks@UMass Amherst. For more information, please contact [scholarworks@library.umass.edu](mailto:scholarworks@library.umass.edu).

PHYSIOLOGICAL MODELS OF *GEOBACTER SULFURREDUCTENS* AND  
*DESULFOBACTER POSTGATEI* TO UNDERSTAND URANIUM REMEDIATION IN  
SUBSURFACE SYSTEMS

A Dissertation Presented

by

ROBERTO ORELLANA ROMAN

Submitted to the Graduate School of the  
University of Massachusetts Amherst in partial fulfillment  
of the requirements for the degree of

DOCTOR OF PHILOSOPHY

September 2014

Microbiology Department

© Copyright by Roberto Orellana Roman 2014  
All Rights Reserved

PHYSIOLOGICAL MODELS OF *GEOBACTER SULFURREDUCENS* AND  
*DESULFOBACTER POSTGATEI* TO UNDERSTAND URANIUM REMEDIATION IN  
SUBSURFACE SYSTEMS

A Dissertation Presented

by

ROBERTO ORELLANA ROMAN

Approved as to style and content by:

---

Derek R. Lovley, Chair

---

Kristen M. De Angelis, Member

---

James F. Holden, Member

---

Jason M. Tor, Member

---

John Lopes, Department Head  
Microbiology

## **DEDICATION**

Para Loreto, Leonor e Ignacio.

*Essentially, all models are wrong, but some are useful.*

George E. P. Box

## ACKNOWLEDGMENTS

I would like to thank Derek Lovley for being a constant source of guidance, critical thinking and support. I arrived to his lab not having idea of anaerobic bacteria and I have learned a lot throughout these years. I would also like to give thanks to my other committee members; Kristen DeAngelis, Jim Holden, and Jason Tor. They have spent many hours discussing the results and have very valuable insights.

Also I thank to several mentors in the lab Carla Risso, Marzia Miletto, and Melissa Barlett that give me support, advice, and motivation. I thank current and past lab members: Arianna Gray, Sean Murphy, Pier Luc Tremblay, Shabir Dar, Dawn Holmes, Ching Leang, Pravin Shrestha, Toshiyuki Ueki, Jo Philips, Nikhil Malvankar, Tunde Mester, Joy Ward, Manju Sharma and Areen Banerjee for valuable help at all stages of this dissertation. Also, I want to thanks to the researchers from other universities that collaborate along this research. Thanks speacially to Luis Comolli (LBNL), Janet Leavitt (UNM), Kim Hixson, and Mary Lipton (PNNL).

I am highly indebted to my friends Burcu Unal, Jennifer Lin and Jesus Alvelo for help in many things and endless support especially when things got tough. I also have special thanks to the administrative people in the department: Maryanne Wells, Sue Laford, Ruthie Allies and Lorell Perreault for the countless times they save me from administrative issues during grad school. Also, I want to thanks to the department head John Lopes for his interesting conversations about science and soccer. I am grateful for all other students in the department that made my time here easier and enjoyable, especially George Hamaoui, Jennifer Hayashi, Joanne Lau, and Sarah Hensley.

Above all, I owe gratitude especially to my wife, my parents and sister. Without their encouragement, patience and love I would not have been capable of finishing this story with a happy end.

**ABSTRACT**  
PHYSIOLOGICAL MODELS OF *GEOBACTER SULFURREDUCENS* AND  
*DESULFOBACTER POSTGATEI* TO UNDERSTAND URANIUM REMEDIATION IN  
SUBSURFACE SYSTEMS

SEPTEMBER 2014

ROBERTO ANDRES ORELLANA ROMAN  
B.A., UNIVERSITY OF CHILE

Ph.D., UNIVERSITY OF MASSACHUSETTS AMHERST

Directed by: Professor Derek R. Lovley

*Geobacter* species are often the predominant Fe(III)-reducing microorganisms in many sedimentary environments due to their capacity for extracellular electron transfer. This exceptional physiological capability allows them to couple acetate oxidation to uranium (U(VI)) reduction, that is one of the most significant interactions between radionuclides and microorganisms that naturally takes place in uranium-contaminated environments. Although this process has been proposed as a promising strategy for the *in situ* bioremediation of uranium-contaminated groundwater, little is known about the molecular mechanisms involved in U(VI) reduction and the interaction between *Geobacter* and other microbial species.

In the first two research chapters, this dissertation aim to study the interaction between *Geobacter sulfurreducens*, a primary model organism to elucidate the physiological capabilities of *Geobacter* species, and U(VI). Our findings presented here suggest that *G. sulfurreducens* requires outer-surface *c*-type cytochromes, but not pili, for



the reduction of uranium, and U(IV), the product of U(VI) reduction was precipitated at the outer cell surface. Our results also suggest that there is not one specific U(VI)-detoxification specific mechanism for uranium detoxification in *G. sulfurreducens*. Rather, resistance to U(VI) appears to be accomplished with multiple stress response systems, that includes detoxification and oxidative stress response, and regulatory networks that facilitate fast adaptation to rapidly changing conditions.

The third research chapter of this dissertation examines the physiology of *Desulfobacter postgatei*, a competitor for acetate during *in situ* bioremediation of subsurface systems at a uranium-contaminated site in Rifle, CO. Our findings suggest that novel enzymatic complexes, such as the energy-converting hydrogenase related complex, Ehr, the proton-translocating ferredoxin:NADP<sup>+</sup> oxidoreductase, Rnf, and also the NADH-dependent reduced ferredoxin:NADP<sup>+</sup> oxidoreductase, Nfn, are involved in energy conservation, making *D. postgatei* a major competitor for acetate in several environments.

# TABLE OF CONTENTS

|  | Page |
|--|------|
| ACKNOWLEDGMENTS .....  | vi   |
| ABSTRACT .....   | vii  |
| LIST OF TABLES .....   | xiii |
| LIST OF FIGURES .....  | xiv  |
|  |      |
| CHAPTER  |      |
|  |      |
| 1. INTRODUCTION .....  | 1    |
| 1.1 Central objective and goals .....  | 1    |
| 1.2 Bioremediation of uranium contamination .....  | 2    |
| 1.3 <i>In situ</i> bioremediation of uranium by microbial reduction .....  | 3    |
| 1.4 <i>Geobacter</i> species .....   | 4    |
| 1.5 Insights of Uranium reduction by <i>Geobacter sulfurreducens</i> .....   | 5    |
| 1.6 Physiological response of <i>G. sulfurreducens</i> to environmental relevant<br>levels of Uranium .....        | 7    |
| 1.7 <i>In situ</i> stimulation of <i>Geobacter</i> towards uranium reduction .....                                 | 7    |
| 1.8 Subsurface microbial ecology during <i>in situ</i> bioremediation of<br>uranium-contaminated groundwater ..... | 8    |
|  |      |
| 2. U(VI) REDUCTION BY A DIVERSITY OF OUTER SURFACE C-TYPE<br>CYTOCHROMES OF <i>GEOBACTER SULFURREDUCTENS</i> ..... | 12   |
| 2.1 Introduction .....   | 12   |
| 2.2 Material and methods .....   | 14   |
| 2.2.1 Bacterial strains, culture conditions, cell suspension .....   | 14   |
| 2.2.2 Transmission electron microscopy .....   | 15   |
| 2.2.3 X-Ray Energy Dispersive Spectroscopy .....   | 16   |
| 2.2.4 Software .....   | 16   |
| 2.2.5 X-Ray Absorption Near Edge Structure (XANES) .....   | 17   |
| 2.2.6 qRT-PCR .....  | 17   |
| 2.3 Results and discussion .....   | 18   |
| 2.3.1 U(VI) Reduction with Genetically Modified Strains .....  | 18   |
| 2.3.2 Speciation and Localization of Uranium .....   | 19   |
| 2.4 Implications .....   | 19   |

|  |    |
|--|----|
| 3. PROTEOME OF GEOBACTER SULFURREDUCENS IN THE PRESENCE OF U(VI).....  | 26 |
| 3.1 Introduction.....  | 27 |
| 3.2 Material and methods.....  | 28 |
| 3.2.1 Strains and culturing .....  | 28 |
| 3.2.2 Protein Digestion and Desalting .....  | 28 |
| 3.2.3 Tandem MS, MS and putative peptide identification .....  | 29 |
| 3.2.4 Determination of Accurate Mass and Time (AMT) Tags.....  | 30 |
| 3.2.5 Impact of mutations on growth in the presence of U(VI).....  | 31 |
| 3.3 Results.....   | 31 |
| 3.3.1 Proteins involved in growth.....   | 32 |
| 3.3.2 Protein and DNA damage .....   | 33 |
| 3.3.3 Detoxification and Membrane damage.....  | 33 |
| 3.3.4 Proteins involved in oxidative stress.....   | 35 |
| 3.3.5 Extracellular matrix proteins.....   | 36 |
| 3.3.6 c-type cytochromes .....   | 36 |
| 3.4 Implications.....  | 37 |
| <br>   |    |
| 4. NOVEL MEMBRANE-BOUND COMPLEXES INVOLVED IN ENERGY CONSERVATION BY THE ACETATE OXIDIZING SULFATE-REDUCING BACTERIUM DESULFOBACTER POSTGATEI..... | 48 |
| 4.1 Introduction.....  | 49 |
| 4.2 Material and methods.....  | 50 |
| 4.2.1 Organism.....  | 50 |
| 4.2.2 Media and cultivation .....  | 51 |
| 4.2.3 Chemostat experiments .....  | 51 |
| 4.2.4 Analytical methods .....   | 51 |
| 4.2.5 DNA extraction and genome sequencing .....   | 52 |
| 4.2.6 Genome annotation .....  | 52 |
| 4.2.7 Metabolic Network Reconstruction .....   | 53 |
| 4.2.8 Total mRNA extraction.....   | 54 |
| 4.2.9 Illumina sequencing and assembly of Illumina reads .....   | 55 |
| 4.2.10 Mapping mRNA reads .....  | 55 |
| 4.3 Results and discussion .....   | 56 |
| 4.3.1 Energy metabolism .....  | 56 |
| 4.3.2 Novel membrane-bound complexes found in the genome of <i>D. postgatei</i> .....  | 57 |
| 4.3.2.1 Qrc (Quinone-reductase) complex.....   | 57 |
| 4.3.2.2 Ehr (Ech-hydrogenase-related) complex .....  | 58 |
| 4.3.2.3 H <sup>+</sup> -translocating ferredoxin:NADP <sup>+</sup> oxidoreductase (Rnf complex) .....  | 60 |
| 4.3.3 <i>In silico</i> metabolic model of <i>D. postgatei</i> .....  | 60 |
| 4.3.4 Growth kinetics and stoichiometry under electron donor and electron acceptor limitation.....   | 61 |
| 4.3.5 Kinetic of acetate oxidation and sulfate reduction.....  | 63 |

|   |     |
|---|-----|
| 4.3.6 Validation of the metabolic model with experimental data .....  | 63  |
| 4.3.7 <i>In silico</i> characterization of <i>D. postgatei</i> metabolism .....   | 65  |
| 4.3.8 Monte Carlo sampling of <i>D.postgatei</i> model.....   | 67  |
| 4.3.9 Genome-wide transcriptional response of <i>D.postgatei</i> to different<br>growth rates.....  | 67  |
| 4.3.10 Implications .....   | 69  |
| <br>  |     |
| 5. CONCLUSION.....  | 81  |
| <br>  |     |
| APPENDICES  |     |
| <br>  |     |
| A. SUPPLEMENTARY INFORMATION U(VI) REDUCTION BY A<br>DIVERSITY OF OUTER SURFACE C-TYPE CYTOCHROMES OF<br>GEOBACTER SULFURREDUCTENS .....  | 85  |
| <br>  |     |
| B. SUPPLEMENTARY INFORMATION PROTEOME OF GEOBACTER<br>SULFURREDUCTENS IN THE PRESENCE OF U(VI) .....  | 89  |
| <br>  |     |
| C. SUPPLEMENTARY INFORMATION NOVEL MEMBRANE-BOUND<br>COMPLEXES INVOLVED IN ENERGY CONSERVATION BY THE<br>ACETATE OXIDIZING SULFATE-REDUCING BACTERIUM<br>DESULFOBACTER POSTGATEI..... | 207 |
| <br>  |     |
| BIBLIOGRAPHY.....   | 371 |

## LIST OF TABLES

| Table  | Page |
|--|------|
| 1. Selected proteins with lower relative abundance during exposure to U(VI) compared to the control cells. ....  | 43   |
| 2. Selected proteins with higher relative abundance during exposure to U(VI) compared to the control cells .....   | 45   |
| 3. Genes that were differentially expressed at least two fold in <i>D. postgatei</i> growing at 0.032 h <sup>-1</sup> compared to those growing at 0.014 h <sup>-1</sup> ..... | 77   |

## LIST OF FIGURES

| Figure | Page  |
|--------|---|
| 1.     | U(VI)-reducing activity of wild type (wt) and mutant strains of <i>G. sulfurreducens</i> ..... 20   |
| 2.     | Uranium LIII-edge XANES spectra of uranium associated with 3 strains of <i>G. sulfurreducens</i> and their corresponding fits..... 21                     |
| 3.     | Proportion of Uranium at the different oxidations states after 4 hours cell suspensions ..... 22  |
| 4.     | TEM pictures showing level of filament production in wild type, $\Delta$ BESTZ and $\Delta$ pilA..... 23  |
| 5.     | CryoTEM images of wild-type reducing fumarate, and wild-type, $\Delta$ pilA, $\Delta$ BESTZ reducing U(VI)..... 24  |
| 6.     | XEDS of wild-type, $\Delta$ pilA, and $\Delta$ BESTZ respiring U(VI) ..... 25   |
| 7.     | Changes in the protein profile as a result of U(VI) exposure ..... 38   |
| 8.     | Effect of U(VI) on the growth of wild-type..... 39  |
| 9.     | Effect of U(VI) on the growth of $\Delta$ sodA ..... 40   |
| 10.    | Effect of U(VI) on the growth of $\Delta$ GSU2212..... 41   |
| 11.    | Effect of U(VI) on the growth of $\Delta$ GSU2213..... 42   |
| 12.    | Comparison of the <i>D. postgatei</i> qrc operon to the one in <i>D. vulgaris</i> , <i>D. autotrophicum</i> , and <i>Desulfosarcina</i> sp. BuS5 ..... 71 |
| 13.    | Representation of quinone reduction by Qrc in H <sub>2</sub> -utilizing SRB and the proposed cytochrome reduction by Qrc in Acetate-utilizing SRB..... 72 |

|     |  |    |
|-----|--|----|
| 14. | Hydrogen cycle in <i>D. vulgaris</i> proposed by Odom and Peck.....                  | 73 |
| 15. | Predicted mechanism of Ehr complex and Qrc complex in <i>D. postgatei</i> .....      | 74 |
| 16. | Schematic metabolic reconstruction of the energy metabolism of <i>D. postgatei</i> . | 75 |
| 17. | Phenotype Phase Planes analysis (PhPP) of <i>D. postgatei</i> metabolic model .....  | 76 |

# CHAPTER 1

## INTRODUCTION

### 1.1 Central objective and goals

Uranium mining, milling, nuclear fuel and weapons manufacturing-related activities have concentrated large quantities of U(VI) in specific areas, resulting in vast zones of contaminated soils and groundwater. Currently, one of the most feasible tools to prevent U(VI) mobility in the environment is *in situ* bioremediation of uranium-contaminated groundwater. This seeks the reduction, by means of microbial respiration, of hexavalent uranium U(VI) to tetravalent uranium U(IV) which is orders of magnitude less soluble. Several sediment-based and *in situ* studies at a uranium-contaminated site in Rifle, CO, have shown that U(VI) reduction can be stimulated with the addition of organic electron donors, such as acetate (1, 2). However a highly efficient and sustainable long-term uranium bioremediation strategy requires a deeper understanding of the *in situ* physiological status of the subsurface community during uranium bioremediation and an identification of the factors potentially limiting U(VI) reduction activity.

The main goal of this dissertation is to address these knowledge gaps by studying the interaction between *Geobacter sulfurreducens* and U(VI) and by studying the physiology of *Desulfobacter postgatei*, its competitor for acetate during *in situ* bioremediation of subsurface systems at a uranium-contaminated site in Rifle, CO.

This project is expected to answer the following research questions:

- i- What are the uranium reductases in *G. sulfurreducens*? Where does U(VI) reduction take place in the cell?
- ii- What is the physiological response of *G. sulfurreducens* in the presence of environmentally relevant concentrations of U(VI)?
- iii- What are the kinetic and stoichiometric parameters that characterize the growth of *Desulfobacter postgatei* under environmental relevant conditions? What are key physiological characteristics that are unknown in the metabolism of *D. postgatei*?



This dissertation is divided into three independent research chapters; each one will correspond to an independent scientific publication. Chapter 1 presents the justification and the background of the study. Chapter 2, 3, and 4, are the main research chapters describing the results and findings from each project. Chapter 2 includes the results about electron transfer mechanism of *Geobacter sulfurreducens* to reduce U(VI), which was recently published (3). Chapter 3 includes the physiological response of *G. sulfurreducens* to environmentally relevant levels of U(VI), which is currently in review by Microbiology Journal. Chapter 4 is devoted to the sulfate-reducing bacteria, *Desulfobacter postgatei* and includes the description of the stoichiometry and kinetics of growth and explores previously unknown metabolic capabilities to conserve energy. Chapter 6 summarizes the findings for the entire study and suggests possible directions for future work.

## **1.2 Bioremediation of uranium contamination**

The use of uranium for nuclear research, fuel production, and weapons manufacturing has resulted in widespread dispersal of an environmental contaminant with a great ecological risk (4). Uranium contamination of sediments and ground/surface water is a serious concern, especially at many former uranium mining and processing facilities (5). At these sites, residual radionuclides have leached into the subsurface threatening the natural environment and human health, both locally and through off-site transport of soluble U(VI) (6). Additional contamination has resulted uranium being released from the combustion of coal as well as from the manufacture and application of phosphate fertilizers (4, 7).

The U.S. Department of Energy's (DOE) Subsurface Science, through the NABIR (Natural and Accelerated Bioremediation Research), EMSP (Environmental Management Science Program), ERSP (Environmental Remediation Sciences Program) and SBR (Subsurface Biogeochemical Research Program) programs, has invested a vast amount of effort to gain a comprehensive and mechanistic understanding of the microbial factors and associated geochemistry controlling uranium mobility in the environment. In several previous studies supported by DOE, a systematic multi-tiered and predictive approach

has been proposed to design strategies for the *in situ* bioremediation of groundwater contaminated with uranium and other toxic metals.

Bioremediation is the application of living or dead organisms to degrade or transform hazardous inorganic and organic contaminants present in the environment (8). It often works by either transforming or degrading contaminants into nonhazardous or less hazardous chemicals. Since, unlike organic compounds, metals and radionuclides cannot be degraded, uranium bioremediation seeks the reduction of U(VI) to U(IV), which is orders of magnitude less soluble than most other U species (9).

There are a number of *ex situ* and *in situ* bioremediation methods currently available. In the *ex situ* approach, also known as “pump and treat methods”, the polluted groundwater is pumped to the surface where it can be treated more easily (10). However, its application in uranium remediation is generally restricted by poor extraction efficiency, the generation of large volumes of toxic uranium waste, and the increased public health and safety risks of bringing uranium contaminants up to the surface (11). On the other hand, the *in situ* approach has been suggested as an attractive alternative strategy for remediation of uranium contaminated subsurface environments due to the fact that is a relatively simple, low cost, effective, and environmentally safe remediation method (7, 11-13). However, this approach still has several challenges. For instance, the addition of extrinsic microbes to the contaminated groundwater may not be a viable option, since foreign microbes may not survive or may not remediate contaminants any better than indigenous microbes (10). Therefore, a significant effort has been made in order to develop and improve the strategies capable to stimulate the indigenous bacteria to reduce mobile U(VI) to the insoluble U(IV). These usually seek to identify the microbes responsible for uranium reduction, expand our understanding about their *in situ* physiological status, enhance the natural microbial environment by adding amendments that make native microbial communities work more effectively towards U(VI) reduction, and integrate the interplay of biology, hydrology, and geochemistry to predictively model the coupled processes in subsurface environments (2, 10, 14).

### **1.3 *In situ* bioremediation of uranium by microbial reduction**

Microbial activity affects the chemical nature of U by altering its solubility, speciation, and sorption properties and thus its bioavailability (15). Some microbes can interact with radionuclides via several mechanisms, some of which may be used as the basis of potential bioremediation strategies. These mechanisms include biosorption, bioaccumulation, biomineralization, microbially enhanced chemisorption and direct enzymatic reduction (16). Among these, the reduction of U(VI) to U(IV) plays a pivotal role in controlling the solubility and mobility of uranium since uraninite,  $UO_2$ , is orders of magnitude less soluble than most other U species (4, 17). Due to its natural occurrence in the environment, applicability, and also due to the greater stability of the reduced form, microbial uranium reduction has become a fundamental baseline behind bioremediation of uranium-contaminated groundwater (16, 18).

The list of bacteria known to reduce U(VI) includes more than 40 species and still is growing (4). Many microorganisms that are able to couple the oxidation of organic compounds to the reduction of Fe(III) are also able to reduce uranium enzymatically (19). Among these, particular attention has been drawn to *Geobacter metallireducens* and *Shewanella putrefaciens* (20) which were the first organisms found to be capable of uranium reduction. Together with *Desulfotomaculum reducens* (21), *Anaeromyxobacter dehalogenans* (22), and *Thermoterrabacterium ferrireducens* (23), they are the only species that can yield enough energy to support growth by uranium reduction. In addition, the sulfate-reducing bacteria *Desulfovibrio desulfuricans*, *D. sulfodismutans*, *D. alaskensis*, *D. vulgaris* and *Desulfomicrobium norvegicum*, and other anaerobes such as *Clostridium* sp. and *Pseudomonas putida* are able to reduce U(VI) enzymatically without conserving energy from these processes (4, 24-28). Nevertheless, other *Geobacter* species, such as *G. lovleyi* and *G. sulfurreducens*, were surprisingly capable to gain enough energy for growth from this process (22).

#### **1.4 *Geobacter* species**

*Geobacter* species are anaerobic iron-reducing bacteria that have received special attention because of their novel electron transfer capabilities. *Geobacter* species have the ability to conserve energy for growth by oxidizing organic compounds coupled to the

reduction of a high variety of electron acceptors (1). This along with its remarkable respiratory versatility (29) allows *Geobacter* to be significant in environments in which Fe(III) reduction is the primary electron-accepting process (30), and more important in many uranium contaminated subsurface environments (7).

*Geobacter sulfurreducens*, a member of the deltaproteobacteria and of the family *Geobacteraceae*, commonly serves as the model organism for the *Geobacteraceae* in subsurface environments. Since it is closely related to *Geobacter* species that are predominant in subsurface environments (31), it has become one of the most intensively studied metal reducing bacteria (1). This was the first *Geobacter* species whose genome was sequenced (31) and for which a genome-based metabolic model was designed and a genetic system was developed (32). Indeed a substantial number of genome-scale gene expression and proteomic studies have been conducted with *G. sulfurreducens* (33-51).

### **1.5 Insights of Uranium reduction by *Geobacter sulfurreducens***

Despite the fact that little is known about the nature of this process, *c*-type cytochromes are expected to play a key role in this process (4, 52). Although the first evidence that *c*-type cytochromes were involved in this process was proposed by Lovley et al (1993) (26, 53), the mechanism(s) by which U(VI) is reduced by *Geobacter* species remains still unknown. In this study, the *c*-type cytochromes were oxidized when U(VI) was added to whole cell suspensions of *Geobacter metallireducens*. Afterwards Lloyd and coauthors (2003)(54) showed that deletion of the gene encoding the periplasmic *c*7 cytochrome, PpcA, negatively impacted acetate-dependent U(VI) reduction in *G. sulfurreducens*. Although this evidence suggested that PpcA may play a role in U(VI) reduction, it did not reveal its specific function. Indeed, more recent studies have shown other *c*-type cytochromes play a key role in microbial U(VI) reduction in *G. sulfurreducens* (55). Shelobolina *et al* found that the elimination of two confirmed outer membrane cytochromes and two putative outer membrane cytochromes significantly decreased the ability of *G. sulfurreducens* to reduce U(VI) by 50–60% (52).

There is an increasing body of evidence that suggest that *c*-type cytochromes are essential molecules for U(VI) reduction in other dissimilatory metal reducing bacteria,

such as *Shewanella* and *Desulfovibrio* species (55, 56). For instance, two studies showed that the periplasmic tetraheme *c3* cytochrome was required for U(VI) reduction by species of the sulfate reducing bacteria, *Desulfovibrio vulgaris* (26) and *Desulfovibrio desulfuricans* (28). It was also reported that the iron reducing bacteria, *Shewanella oneidensis* MR-1 mutant lacking the cytochrome *c552* was deficient in its ability to reduce U(VI) (57). Furthermore, it was shown that the failure to complete *c*-type cytochromes maturation impaired U(VI) reduction. Indeed, the deletion of *mtrC* and *omcA*, both outer membrane bound decaheme *c*-type cytochrome, affected significantly U(VI) reduction (55). More interestingly, the same research shows both cytochromes forming a close association with extracellular uranium nanoparticles within EPS.

Despite the different lines of evidence that support an important role of *c*-type cytochromes in U(VI) reduction, it has recently been suggested by others that electrons are directly transferred from the conductive pili of *G. sulfurreducens* (58, 59) to U(VI) (60, 61). Although this evidence contrasts with the finding that pili are not required for the reduction of other soluble extracellular electron acceptors such as Fe(III) citrate or the humic substances analog anthraquinone-2,6-disulfonate (AQDS) (58, 62), further experiments are necessary to resolve this controversy.

Not only are the mechanisms of *G. sulfurreducens* to reduce U(VI) still unclear, but also the site where this reaction occurs remains unknown. Since extracellular electron transfer to minerals, such as Fe(III) and Mn(IV) oxides (20, 29, 63), electrodes (64), and soluble metal species, such as Fe(III) chelated with citrate (65) have been described as one of *Geobacter*'s specialties, it has been assumed that U(VI) reduction mainly takes place at the outer membrane (52). However, contradictory results have hampered our understanding about the location of U(VI) reduction.

Initially, chymotrypsin-treated cells performed uranium reduction at similar rates as untreated cells, while the rate of reduction of insoluble Fe(III) oxides was reduced by 90% (16). Assuming that the chymotrypsin treatment was able to efficiently digest all outer membrane proteins, these results suggested that surface proteins are required for electron transfer to Fe(III) oxides, but not U(VI). In spite of this, more recent studies also suggested a role for periplasmic cytochromes as putative electron shuttles, from central metabolism to the outer membrane, and outer membrane cytochromes as the uranyl

reductases (52). A more compelling argument was revealed in the same study, showing that accumulation of uranium in the periplasm of U(VI) reduction-impaired mutants and wild type. This implies that periplasmic uranium accumulation observed before is unrelated to the capacity for uranium reduction and may instead reflect the ability of uranium to penetrate the outer membrane and react with substances in the periplasm that promote formation of precipitates. Although *Geobacter* species has been identified as an effective means for immobilizing U(VI) in several bioremediation engineered systems, the biomolecular mechanisms of U(VI) reductions by *Geobacter* species are still not well understood.

### **1.6 Physiological response of *G. sulfurreducens* to environmental relevant levels of U(VI)**

U(VI) is both biochemically and radiologically toxic even for microorganisms that use it as a source of energy (4, 66). Despite of its importance as a model to expand the understanding of *in situ* bioremediation of U(VI) contaminated groundwater, the knowledge about the interaction between *Geobacter sulfurreducens* and U(VI) is still highly limited.

There are few studies addressing the effects of U(VI) exposure to anaerobic pure bacterial cultures, and none of them includes *Geobacter* species (67, 68). These studies reported that, in contrast to essential metals that can be imported or extruded depending on current requirements of the cell (69), U(VI) presents a particular challenge to *Geobacter* species. Since there is no evidence for U(VI)-specific transport or protective mechanism, there are many other unspecific physiological traits that may deal with U(VI). Also, the capacity of U(VI) to denature proteins, inactivate functional groups of enzymes, disrupt the cell envelope, and damage DNA remains unknown (70-72).

### **1.7 *In situ* stimulation of *Geobacter* towards uranium reduction**

Initially supported by the The Natural and Accelerated Bioremediation Research (NABIR) program, several efforts have been made to study the potential for stimulating

indigenous U(VI)-reducing microbial communities in subsurface sediments. Early studies evaluated which electron donors might best promote the activity of dissimilatory metal-reducing microorganisms that would reduce the available uranium in subsurface sediments, and which species were the predominant members of the microbial community (12, 31). In these studies, subsurface sediments from a variety of uranium-contaminated sites were incubated under anaerobic conditions with various electron donors added while monitoring metal reduction and microbial community composition over time. In nearly all cases, species belonging to the *Geobacteraceae* became the predominant metal-reducing microorganisms (73, 74). Afterwards, several studies have shown the same predominance of *Geobacter* in the field (7, 30, 75, 76) demonstrating that laboratory incubations of uranium-contaminated sediments yielded useful insights into the microbial processes likely to take place *in situ*.

Another important outcome of the laboratory sediment incubations was that acetate was shown to be the best promoter for microbial metal reduction without stimulating the unwanted growth of fermentative organisms that were not involved in the uranium reduction process and may cause aquifer clogging. These results served as the basis for the design of field experiments at the uranium-contaminated Uranium Mill Tailings Remedial Action (UMTRA) Project site in Rifle, Colorado. These field scale studies have demonstrated the stimulation of uranium bioremediation with added acetate was a repeatable phenomenon and that U(VI) reduction was clearly linked to the presence and activity of microorganisms of the family *Geobacteraceae* (7, 74). The field scale studies indicate an increase in *Geobacter* species by several orders of magnitude in groundwater accompanied by enhanced uranium and Fe (III) reduction for up to 40 days. Furthermore, it was reported that vanadium was also removed from the groundwater via the reduction of V(V) to V(IV), which is consistent with our other work supported by NABIR that *Geobacter* species are also capable of V(V) reduction (77).

## **1.8 Subsurface microbial ecology during *in situ* bioremediation of uranium-contaminated groundwater**

The success of the *in situ* stimulation approach depends on ensuring iron reduction as the predominant terminal electron-accepting process (TEAP) and uranium-reducing bacteria, such as *Geobacter*, as the dominant species in the subsurface for the longest possible time. Although, the first *in situ* experiment reported that *Geobacter* was successfully stimulated for 30-40 days (7), continuing acetate injections at the Rifle field site from year to year have shown that the initial *Geobacter* bloom only lasted for 20 days in subsequent experiments in the same plot and was followed by a more rapid decline of the *Geobacter* and increase of sulfate-reducing bacteria (SRB) (75). Once the sulfate reduction phase had begun, uranium removal was less effective suggesting that the acetate-consuming sulfate-reducing bacteria, such as members of *Desulfobacteraceae* and some Firmicutes present at Rifle site, may not be able to reduce uranium (78). Geochemical monitoring and molecular analysis in sediments and groundwater have shown that due to the high concentrations of sulfate (~8-10 mM), complete oxidizing sulfate-reducing bacteria were able to consume the acetate, thereby limiting the activity of the *Geobacter* and decreasing the overall effectiveness of uranium removal (7). It raises the point that during acetate-amended bioremediation, *Geobacter* must compete for acetate with SRB.

Since Fe(III) reduction is energetically more favorable than  $\text{SO}_4^{2-}$  reduction, iron-reducing bacteria were expected to outcompete SRB for common electron donors (79). Therefore, it was hypothesized that Fe(III) depletion was the main factor driving the shift from dissimilatory iron reduction to sulfate reduction as the dominant TEAP. To test this hypothesis, microcosm and column studies were conducted using Rifle sediments. These results suggested that both TEAP processes can take place concurrently, even after long periods of acetate amendment, and the lack of Fe(III) availability may not be the primary reason for the *Geobacteraceae* decline (80). Therefore, the mechanism of interaction between the *Geobacter* and SRB is still unknown, and thus supporting the hypothesis that this might be more complex than a competitive thermodynamic interaction.

Due to the advantages of acetate-amended based bioremediation, our current interest in uranium remediation is primarily focused on the interactions of these two specific microbial groups and the significance of their interaction to remediation



strategies. During 2008 and 2009 *in situ* field studies, the diversity, abundance, and metabolic state of the sulfate-reducing community was investigated to better understand the microbial community dynamics involved in the transition from iron to sulfate reduction. Clone libraries based on the *dsrAB* gene, which encode  $\alpha$  and  $\beta$  subunits of the dissimilatory (bi)sulfite reductase, indicated that there were three major phylogenetic clusters of SRB at the site: *Desulfobacteraceae*, *Desulfobulbaceae*, and the *Syntrophaceae*-related sulfate reducers. The *Desulfobacteraceae* cluster displays 97% sequence similarity with *Desulfobacter postgatei* (78). The recovered *dsrAB* sequences were used to design primers to assess the abundance and metabolic state of the sulfate-reducing community from estimates of *dsrAB* operon and transcript abundance, respectively. During the sulfate reduction phase the *Desulfobacteraceae*-related SRB were found at an order of magnitude greater abundance than the *Desulfobulbaceae*- and *Syntrophaceae*-related SRB (78). Similarly, the *Desulfobacteraceae* cluster was found to be the most active, as the number of *dsrAB* transcripts was 2 orders of magnitude higher than that of *Desulfobulbaceae* and *Syntrophaceae* clusters (78). More recent studies agreed with these results suggesting that the diversion of acetate flux from *Geobacter* species to *Desulfobacter postgatei* is a likely explanation for the poor performance of the uranium bioremediation strategy under sulfate-reducing conditions (81, 82).

*Desulfobacteraceae* are the most important players during the sulfate reduction phase. Therefore, the next step to improving remediation strategies is to determine the mechanisms of interaction between these and the *Geobacter* species and ascertain possible changes to the current strategy to improve long-term uranium reduction. However, since no field isolates of acetate-using SRB from the *Desulfobacteraceae* have been cultured, the *Desulfobacter postgatei* strain 2ac9 was used as model organism to get a better understanding of its metabolic potential that drives microbial interactions between *Geobacter* and SRB communities during uranium bioremediation. The availability of *D.postgatei* genome sequence will help to design genome-wide studies to elucidate and compare its global physiological status *in situ* and laboratory incubations. Moreover, together with the availability of genome sequences of relevant *Geobacteraceae* species in Rifle (83), information on the *D. postgatei* genome was

utilized to design a computational metabolic model that can predict the physiological responses under environmental relevant conditions.

## CHAPTER 2

### U(VI) REDUCTION BY A DIVERSITY OF OUTER SURFACE C-TYPE CYTOCHROMES OF *GEOBACTER SULFURREDUCTENS*

#### 2 Abstract

Early studies with *Geobacter sulfurreducens* suggested that outer-surface *c*-type cytochromes might play a role in U(VI) reduction, but it has recently been suggested that there is substantial U(VI) reduction at the surface of the electrically conductive pili known as microbial nanowires. This phenomenon was further investigated. A strain of *G. sulfurreducens*, known as Aro-5, which produces pili with substantially reduced conductivity, reduced U(VI) nearly as well as wild-type as did a strain in which the gene for PilA, the structural pilin protein, was deleted. In order to reduce rates of U(VI) reduction to levels less than 20% of wild-type it was necessary to delete the genes for the five most abundant outer surface *c*-type cytochromes of *G. sulfurreducens*. X-ray absorption near-edge structure spectroscopy demonstrated that whereas  $83 \pm 10\%$  of the uranium associated with wild-type cells correspond to U(IV) after four hours of incubation, with the quintuple mutant  $89 \pm 10\%$  of uranium was U(VI). Transmission electron microscopy and X-ray Energy Dispersion Spectroscopy revealed that wild-type cells did not precipitate uranium along pili as previously reported, but U(IV) was precipitated at the outer cell surface. These findings are consistent with previous studies which have suggested that *G. sulfurreducens* requires outer-surface *c*-type cytochromes, but not pili, for the reduction of soluble extracellular electron acceptors.

#### 2.1 Introduction

The mechanisms for U(VI) reduction in *Geobacter* species are of interest because the precipitation of U(VI) to U(IV) is a promising strategy for the *in situ* bioremediation of uranium-contaminated groundwater and *Geobacter* species often predominate in subsurface environments in which U(VI) reduction is stimulated with the addition of organic electron donors (2, 37). The suggestion that electrons are directly transferred from the conductive pili of *Geobacter sulfurreducens* to U(VI) (60, 61) contrasts with the

finding that pili are not required for the reduction of other soluble extracellular electron acceptors such as Fe(III) citrate or the humic substances analog anthraquinone-2,6-disulfonate (AQDS) (58, 62).

Pili are required for long-range electron transport to insoluble electron acceptors in the *Geobacter* species that have been examined to date. This includes reduction of insoluble Fe(III) oxides (58, 84) and electron exchange between syntrophic partners (35, 85) as well as electron conduction through current-producing biofilms (59, 86, 87). This has been attributed to the metallic-like conductivity of the pili (59, 88). For example, a strain of *G. sulfurreducens*, designated Aro-5, which was genetically modified to produce pili with diminished conductivity lacked the capacity for effective Fe(III) oxide reduction and current production (88). In addition to pili, *G. sulfurreducens* requires the multi-heme *c*-type cytochrome, OmcS, for Fe(III) oxide reduction (89). OmcS is specifically localized on the pili (90). Thus, the simplest model for the last steps in Fe(III) oxide reduction is electron transport to OmcS via the pili, with OmcS facilitating electron transfer from the pili to Fe(III) oxide (91, 92). In a similar manner, networks of pili facilitate long-range electron transport through conductive biofilms of *G. sulfurreducens*, but one or more multi-heme cytochromes are required to promote electron transfer from the biofilm to electrodes (87, 93, 94).

Gene deletion studies demonstrated that, in contrast to the requirement of OmcS for Fe(III) oxide reduction, OmcS was not essential for the reduction of Fe(III) citrate or AQDS (62, 89), consistent with the ability of the pili-deficient strain to reduce these electron acceptors (58, 62). In order to significantly reduce the capacity for AQDS reduction it was necessary to delete the genes for five outer-surface *c*-type cytochromes in one strain (58, 62). These included OmcS and the OmcS homolog OmcT, as well as OmcE, OmcZ, and OmcB. Immunolabelling studies have demonstrated that OmcB is embedded in the outer membrane of *G. sulfurreducens* with a portion of the molecule exposed to the extracellular environment (95), whereas as OmcZ (94) and OmcE (89) are localized in the extracellular matrix. The necessity to remove all of these cytochromes suggested that AQDS reduction is rather non-specific. Although deleting just OmcB significantly eliminated the capacity for Fe(III) citrate reduction (96) the OmcB-deficient

mutant adapted over time to reduce Fe(III) citrate in the absence of OmcB with increased expression of other outer-surface cytochromes (97).

A diversity of *c*-type cytochromes can reduce U(VI) *in vitro* (55, 93, 98, 99). Furthermore, *c*-type cytochromes are essential for U(VI) reduction in *Shewanella oneidensis*, which accumulates uranium nanoparticles in association with the outer membrane cytochromes (55). Previous studies also suggested that *c*-type cytochromes exposed on the outer surface of *G. sulfurreducens* were involved in U(VI) reduction (52). An important line of evidence for a potentially important role of pili in U(VI) reduction was the finding that a pilA-deficient mutant reduced U(VI) at a rate ca. one-third the rate that wild-type reduced U(VI) (60). However, the pilA-deficient mutant was also defective in the production of outer-surface *c*-type cytochromes (60), confounding interpretation of the results. These considerations, and the recent availability of the Aro-5 strain, led us to further investigate the hypothesis that pili are a major conduit for electron transfer to U(VI) by *G. sulfurreducens*.

## 2.2 Material and methods

### 2.2.1 Bacterial strains, culture conditions, cell suspensions

All strains (Table A1) were obtained from our laboratory collection and were routinely cultured anaerobically in medium with 10 mM acetate as electron donor and 20 mM fumarate as electron acceptor, as previously described (52).

Resting cell suspensions were prepared as previously described (52). Briefly, cells were harvested in late exponential phase with an optical density of 0.25-0.28, washed with buffer and resuspended in buffer containing NaHCO<sub>3</sub> (2.5 g L<sup>-1</sup>), NH<sub>4</sub>Cl (0.25 g L<sup>-1</sup>), NaH<sub>2</sub>PO<sub>4</sub>·H<sub>2</sub>O (0.006 g L<sup>-1</sup>), and KCl (0.1 g L<sup>-1</sup>) at an OD<sub>600</sub> of 0.075-0.08. Acetate (5mM) and uranyl acetate (1mM) were added as electron donor and acceptor, respectively. Heat-killed controls were prepared by autoclaving the cell suspension for 30 min before the addition of U(VI). Cell suspensions were incubated at 30 °C.

The ability of cells to reduce U(VI) was monitored as the loss of U(VI) over time as previously described (52). Briefly, samples from cell suspensions (100 ul) were taken at

one-hour intervals and diluted in 14.9 ml of anoxic 100 mM bicarbonate and 14.9 ml of anoxic URAPLEX working solution. U(VI) concentrations were quantified with Kinetic Phosphorescence Analyzer (KPA) (Chemcheck Corp., Richland, WA), and the rate of enzymatic U(VI) reduction over 4 h was calculated as described previously (52).

### **2.2.2 Transmission electron microscopy**

For a control survey of cell appendages, cells were harvested by centrifugation at mid-log phase and prepared as previously described (52). Samples were placed on 400-mesh carbon-coated copper grids, incubated for 5 minutes, and then stained with 2 % uranyl acetate. Cell appendages were observed with a JEOL 100 transmission electron microscope at an accelerating voltage of 80 kV. Images were taken digitally using the MaxIm-DL software and analyzed using Image J (<http://rsbweb.nih.gov/ij/index.html>).

For cryo-TEM, 5  $\mu$ L aliquots of culture were placed onto lacey carbon grids (Ted Pella 01881, Ted Pella Inc., Redding, CA) that were pre-treated by glow-discharge. The Formvar support was not removed from the lacey carbon. The grids were manually blotted with filter paper and flash frozen with a portable cryo-plunger (100), and stored in liquid nitrogen.

For air-dried samples aliquots of 5  $\mu$ L were placed onto continuous carbon-coated Formvar TEM grids (Ted Pella 01753, Ted Pella Inc., Redding, CA) pre-treated grids by glow-discharge. They were blotted after equilibration for 2 min. Cryo-grids were freeze-dried after cryo-TEM imaging. Both air-dried and freeze dried cryo-TEM specimens were used for XEDS analysis as described below.

Cryo-TEM images were acquired on a JEOL-3100-FFC electron microscope equipped with a FEG electron source operating at 300 kV, an Omega energy filter, cryo-transfer stage, and a Gatan 795 4Kx4K CCD camera mounted at the exit of an Electron Decelerator held at a constant voltage of 200 kV (101). The stage was cooled with liquid nitrogen to 80 K during acquisition of all data sets. In order to have a statistically relevant survey, over 100 images were recorded using magnifications of 112Kx, 70Kx, and 42Kx at the CCD giving a pixel size of 0.14 nm, 0.21 nm or 0.375 nm at the specimen, respectively. Underfocus values ranged between 2  $\mu$ m  $\pm$  0.5  $\mu$ m to 12  $\mu$ m  $\pm$  0.5  $\mu$ m, and

energy filter widths were typically around  $28 \text{ eV} \pm 2 \text{ eV}$ . The survey of the grids and the selection of suitable targets for tilt series acquisition were done in low dose diffraction mode through the acquisition of dozens of images.

Two tomographic data sets of  $\Delta$ pilA were acquired. Tomographic tilt series were acquired under low dose conditions, over an angular range between  $+62^\circ$  and  $-62^\circ$ ,  $\pm 2^\circ$  with increments of  $2^\circ$ . Sixty (60) and sixty three (63) images were recorded for these tilt series, acquired semi-automatically with the program Serial-EM (<http://bio3d.colorado.edu/>) adapted to JEOL microscopes. For these tilt series data sets, images were recorded using nominal magnification of 15 kx resulting in 42 kx at the CCD and a pixel size of 0.375 nm at the specimen. The under focus value was set to  $12 \mu\text{m} \pm 0.5 \mu\text{m}$ , and energy filter widths to 28 eV. The maximum dose used per complete tilt series was approximately  $140 \text{ e}^-/\text{\AA}^2$ .

### **2.2.3 X-Ray Energy Dispersive Spectroscopy**

High spatial resolution chemical analyses of cell membranes of air-dried samples on continuous carbon-coated Formvar TEM grids and freeze-dried cryo-TEM samples were carried out in the JEOL 2100-F 200 kV Field-Emission Analytical Transmission Electron Microscope (TEM) equipped with Oxford INCA Energy Dispersive Spectroscopy (EDS) X-ray detection system at the Molecular Foundry at Lawrence Berkeley National Laboratory. High angle annular dark field (HAADF) scanning transmission electron microscopy (STEM) images and X-ray elemental line scans were acquired with a 1 nm probe at 120 or 200 kV. The specimens were tilted 10 degrees toward the X-ray detector to optimize the X-ray detection geometry. Collection times were 300 live seconds for each line scan. The EDS line scans on the high contrast regions of the outer membrane clearly demonstrate the localized uranium in this membrane responsible for the increased contrast in the STEM HAADF images.

### **2.2.4 Software**

All tomographic reconstructions were obtained with the program Imod (<http://bio3d.colorado.edu/>) (102). The program ImageJ (NIH, <http://rsb.info.nih.gov/ij/>)

was used for analysis of the 2D image projections. Volume rendering and image analysis of tomographic reconstructions was performed using the open source program ParaView (<http://www.paraview.org/>) and movies were created with the open source package ffmpeg (<http://www.ffmpeg.org/>). The inner membranes of 2 cells of each species were segmented by hand using the program Imod.

### **2.2.5 X-Ray Absorption Near Edge Structure (XANES) Analyses**

The oxidation state of uranium in cell suspensions samples was determined with the X-ray Absorption Near Edge Structure (XANES) spectroscopic method. Cell pellets from the cell suspensions were flash frozen in liquid nitrogen, and shipped on ice. Samples were loaded in Aluminum sample holder with Kapton windows in an anaerobic chamber (2-5% hydrogen, balance nitrogen) at the Stanford Synchrotron Radiation Lightsource (SSRL, SLAC National Accelerator Laboratory, Menlo Park, CA). Immediately prior to analysis, the sample assembly was mounted in a liquid nitrogen cryostat, placed under vacuum, and frozen. U L<sub>III</sub>-edge transmission spectra were collected at SSRL beamline 4-1, using a Si (220) double-crystal monochromator detuned to reject higher harmonic intensity. Vertical slits in the experimental hutch were set to 0.5 mm during the measurement to insure that the spectrometer resolution was lower than that of the intrinsic core-hole lifetime limitation. Energy calibration was monitored continuously and no drift was detected. XANES spectra were background subtracted and analyzed using ATHENA software (103).

### **2.2.6 qRT-PCR**

Total RNA was extracted with RNeasy Mini kit (Qiagen) from mid-log acetate-fumarate cultures. cDNA was generated with the Enhanced Avian First Strand Synthesis Kit (Sigma-Aldrich, St-Louis, MO, USA) using random primers according to manufacturer's recommendations. The SYBR Green PCR Master Mix (Applied Biosystems, Foster City, CA) and the ABI 7500 Real-Time PCR System were used to amplify and to quantify PCR products from *pilA* with RT\_ORF02545\_F and



RT\_ORF02545\_R pair of primers (87). Expression of this gene was normalized with proC expression, a constitutively expressed gene in *G. sulfurreducens* using proC2F and proC77R pair of primers. Relative levels of expression of the studied genes were calculated by the  $2^{-\Delta\Delta CT}$  method (76).

## 2.3 Results and Discussion

### 2.3.1 U(VI) Reduction with Genetically Modified Strains

Strain Aro-5, which produces pili with diminished conductivity, but still properly localizes outer surface *c*-type cytochromes (88), reduced U(VI) at rates that were only slightly lower and not significantly different than the wild-type rate of 0.23  $\mu\text{M}$  of U(VI)  $\text{mg}^{-1} \text{min}^{-1}$  (Figure 1). This result suggested that electron conduction along pili was not an important requirement for U(VI) reduction.

With further investigation, we could not replicate the previously reported findings (60) that the *pilA*-deficient mutant had substantially lower rates of U(VI) reduction than wild-type or that pre-growing cells at 25 °C, a temperature suggested to increase pili production (60) significantly enhanced U(VI) reduction (Figure 1).

Previous studies on the mechanisms for the reduction of anthraquinone-2,6-disulfonate (AQDS), another soluble extracellular electron acceptor, demonstrated that deletion of the genes for multiple outer-surface *c*-type cytochromes was necessary in order to substantially diminish rates of AQDS reduction (62). In a similar manner, deletion of genes of the outer-surface *c*-type cytochromes, OmcB or OmcE, only partially reduced rates of U(VI) reduction (52). A quadruple mutant deficient not only in OmcB and OmcE, but also the outer-surface cytochromes OmcS, and OmcT, still reduced U(VI) at rates (40%) of wild-type (Fig. 1). A quintuple mutant in which *omcZ* was deleted along with *omcB*, *omcE*, *omS*, and *omcT* ( $\Delta\text{BESTZ}$ ) only reduced U(VI) at a rate 19% that of wild-type (Fig. 1). This could not be attributed solely to the loss of OmcZ, because a strain in which only *omcZ* was deleted reduced U(VI) at a rate ca. 50% of wild-type (Fig. 1).

Lower rates of U(VI) reduction in the quintuple mutant could not be attributed to an impact on pili production. Transcript abundance of *pilA* relative to the housekeeping gene *proC* was 3.5 ( $\pm 0.76$ ) fold higher in the quintuple mutant than wild-type cells and transmission electron microscopy revealed the expression of pili in the quintuple mutant and wild-type, but not in the *pilA*-deficient mutant (Figures 4 and A1).

### 2.3.2 Speciation and Localization of Uranium

Analysis of cell pellets from the cell-suspension incubations with X-ray absorption near-edge structure spectroscopy (XANES) demonstrated that after 4 hours,  $83 \pm 10\%$  of the uranium associated with wild-type cells was U(IV) with the remainder in the U(VI) oxidation state (Figure 2). The percentage of U(IV) was slightly lower in the *pilA* mutant ( $63 \pm 10\%$ ), but the difference was not significantly different. In contrast,  $89 \pm 10\%$  of uranium was present as U(VI) in the quintuple mutant (Figure 3).

In contrast to previous reports (60), no U(IV) precipitates associated with the pili of wild-type cells were observed (Figure 5). There was an electron-dense accumulation at the outer membrane of both wild-type and *pilA* mutant, which X-ray Energy Dispersion Spectroscopy (XEDS) confirmed was uranium (Figure 6 and Fig. A2). These precipitates were not detected in cell suspensions provided fumarate rather than U(VI) as an electron acceptor (Fig. 5). There was very little accumulation of uranium on the outer-surface of the quintuple mutant, consistent with the low levels of U(VI) reduction.

### 2.4 Implications

The results suggest that *G. sulfurreducens* reduces U(VI) much like it reduces AQDS, another soluble, extracellular electron acceptor. A number of outer-surface *c*-type cytochromes appear to contribute to U(VI) reduction. This is analogous to results in *Shewanella oneidensis* (55). Previous results have demonstrated that *G. sulfurreducens* *c*-type cytochromes reduce U(VI) *in vitro*, including OmcS and OmcZ (93, 98). Long-range electron conduction through pili is not necessary for the reduction of other soluble

electron acceptors by *G. sulfurreducens* (58) and is also not expected to be necessary for the reduction of U(VI).

**Figures:**

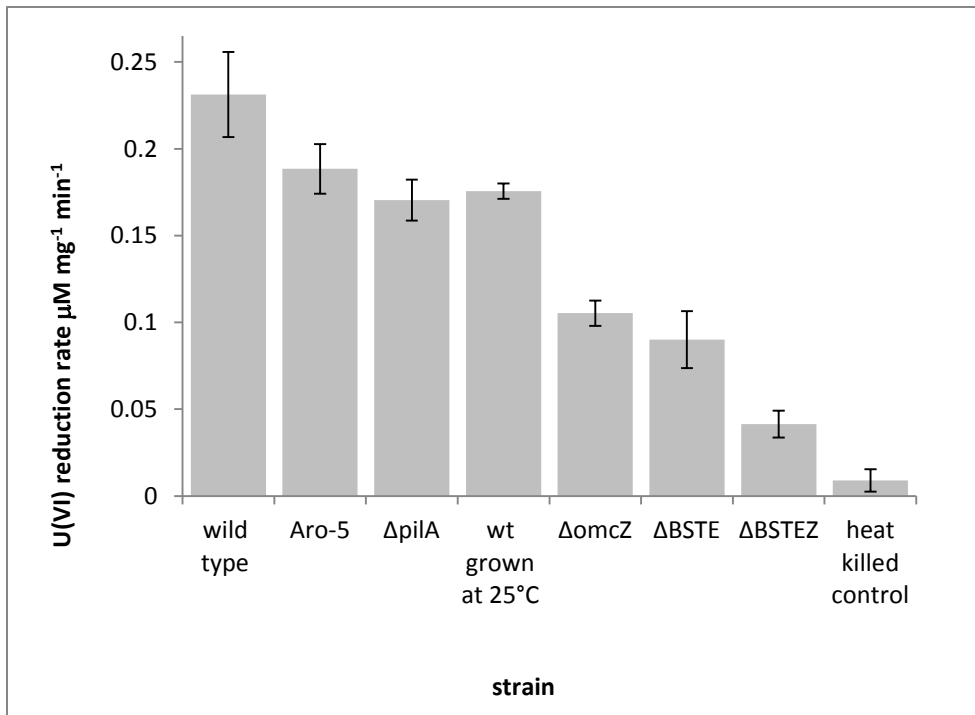


Figure 1: U(VI)-reducing activity of wild type (wt) and mutant strains of *G. sulfurreducens*. Data are means  $\pm$  standard deviations (SD) of triplicates.

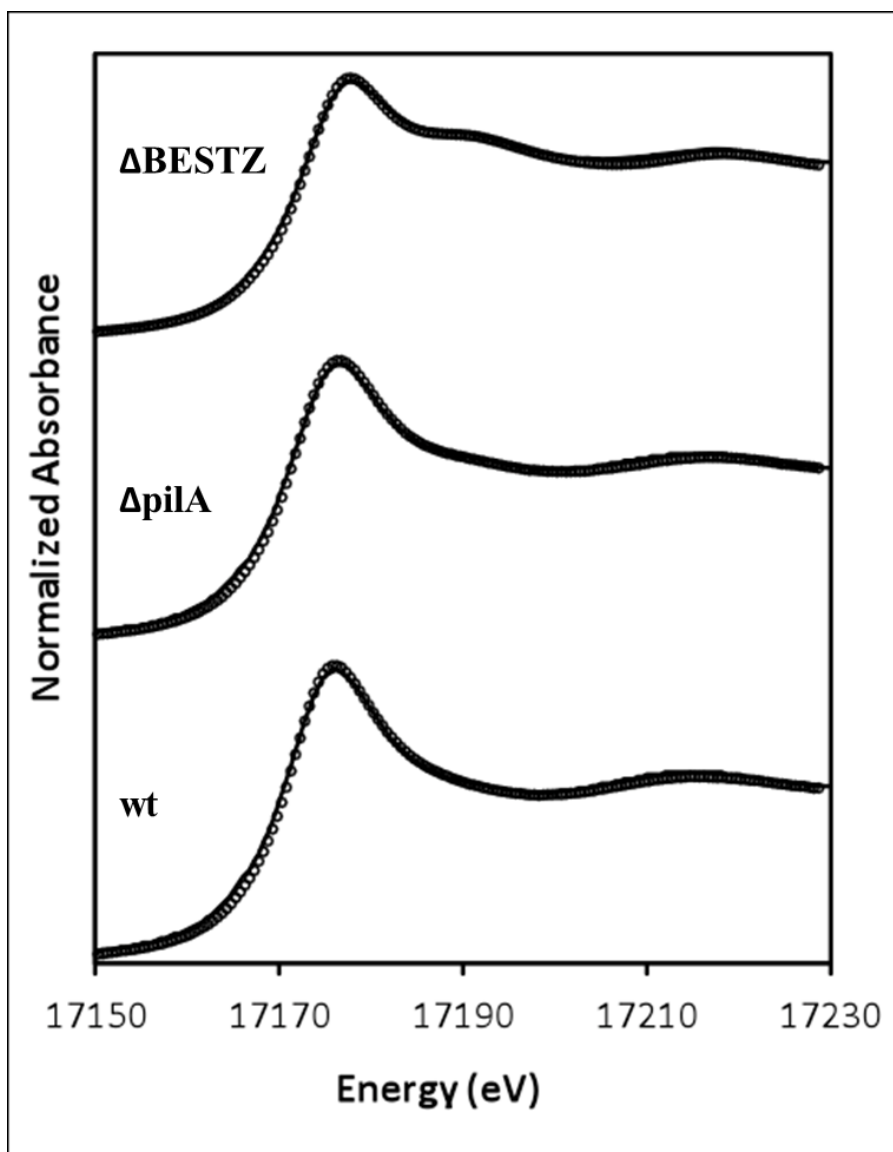


Figure 2: Uranium LIII-edge XANES spectra of uranium associated with 3 strains of *G. sulfurreducens* (circles) and their corresponding fits (lines).

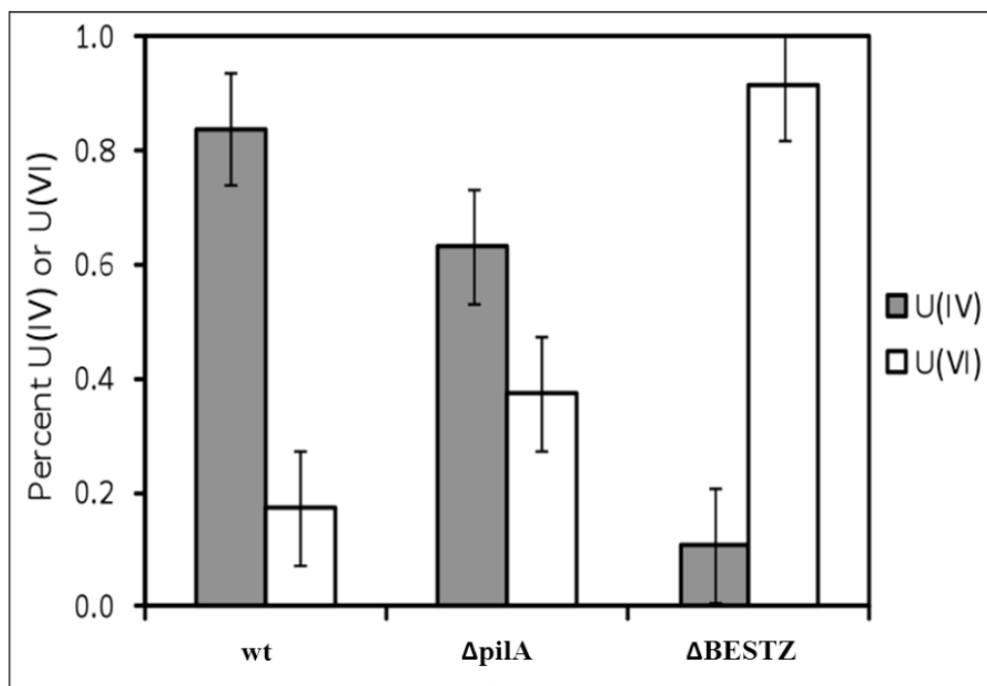


Figure 3: Proportion of Uranium at the different oxidations states: U(IV), gray bars, and U(VI), white bars, after 4 hours cell suspensions.

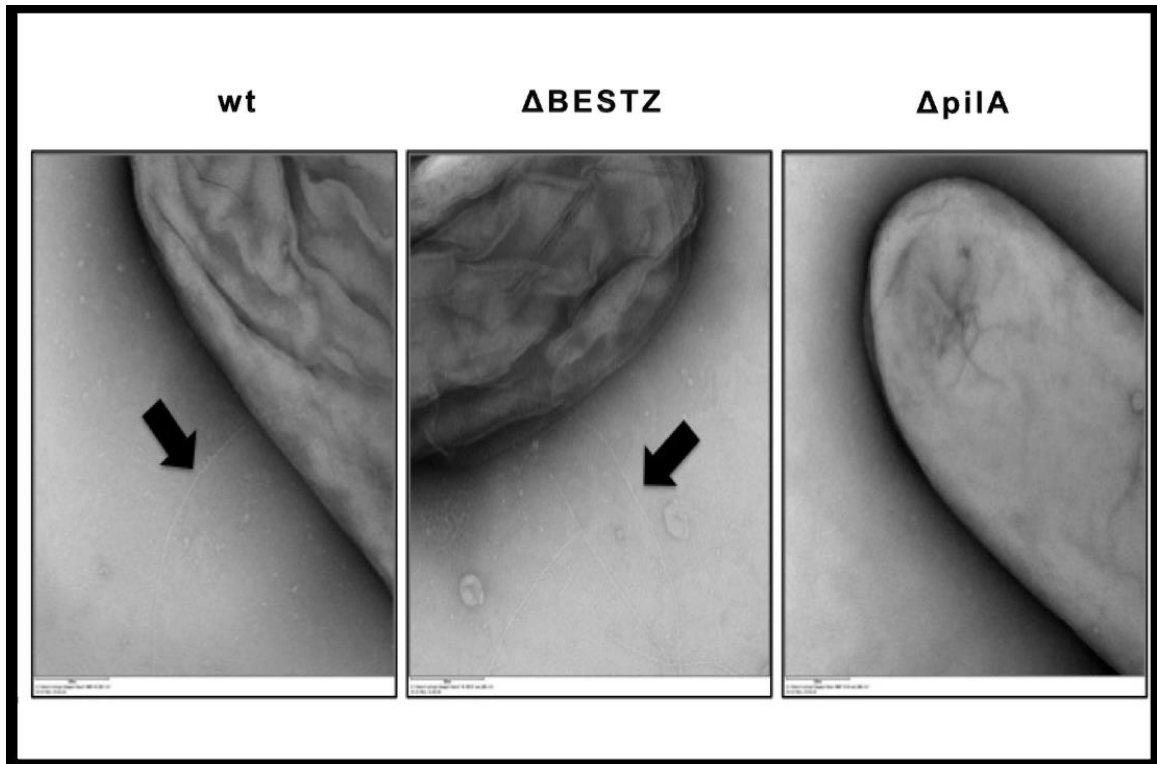


Figure 4: TEM pictures showing level of filament production in wild type(left),  $\Delta$ BESTZ(middle) and  $\Delta$ pilA(right).

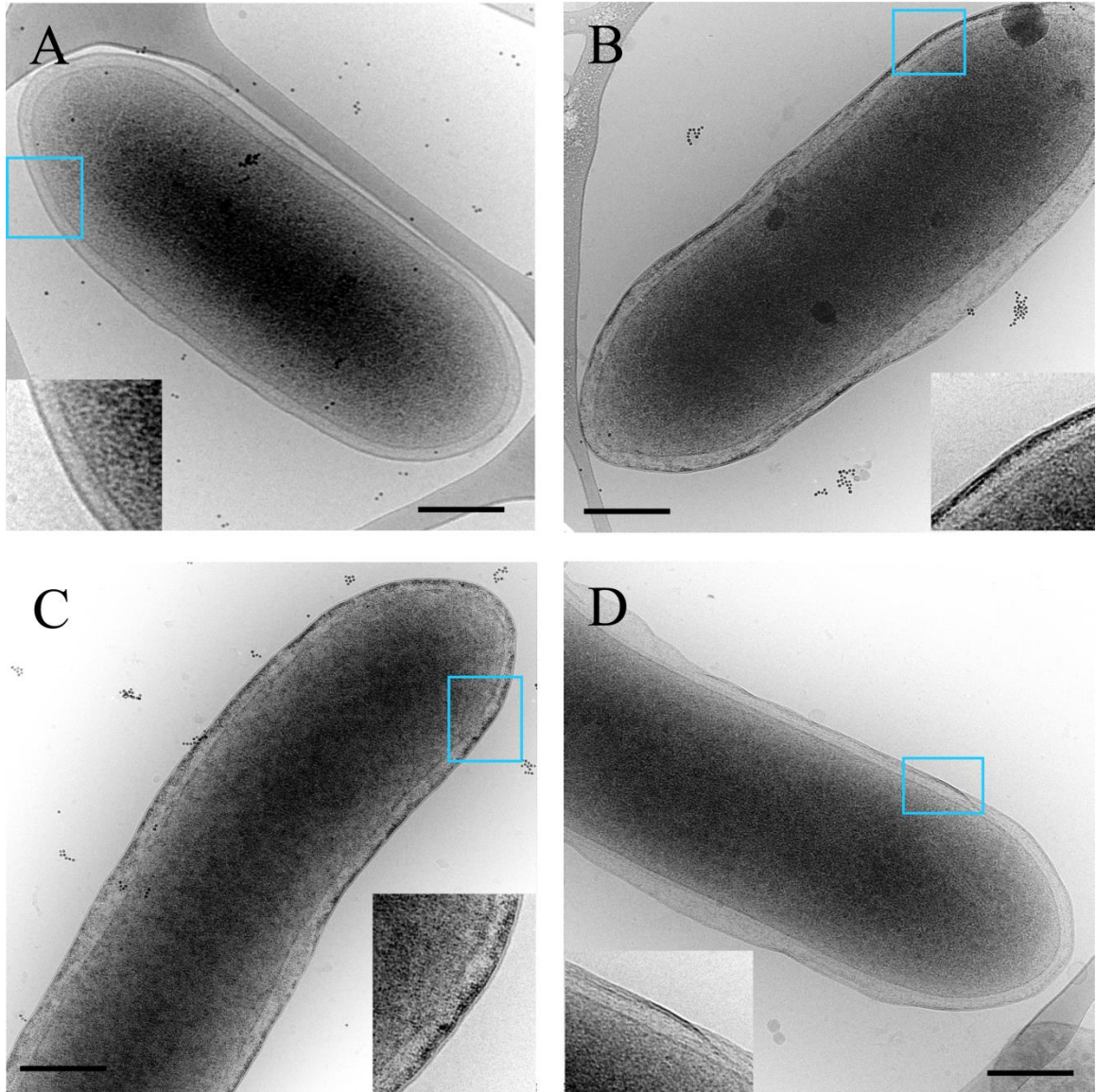


Figure 5: (A) CryoTEM images of wild-type reducing fumarate, and (B) wild-type, (C)  $\Delta pilA$ , (D)  $\Delta BESTZ$  reducing U(VI). (A) The cell wall of *Geobacter* respiring in fumarate is typical of gram-negative bacteria with clear inner and outer membrane and a transparent periplasmic space. (B) and (C): The cell walls of wild-type and  $\Delta pilA$  are spanned by irregular patches of high contrast (electron dense) material, mainly at the outer membrane. (D) The cell wall of  $\Delta BESTZ$  respiring U(VI) appears to contain significantly less high contrast aggregated material and is closer to wild-type respiring fumarate. On occasion there are irregular patches of aggregates as seen in the inset. Scale bar: 250 nm.

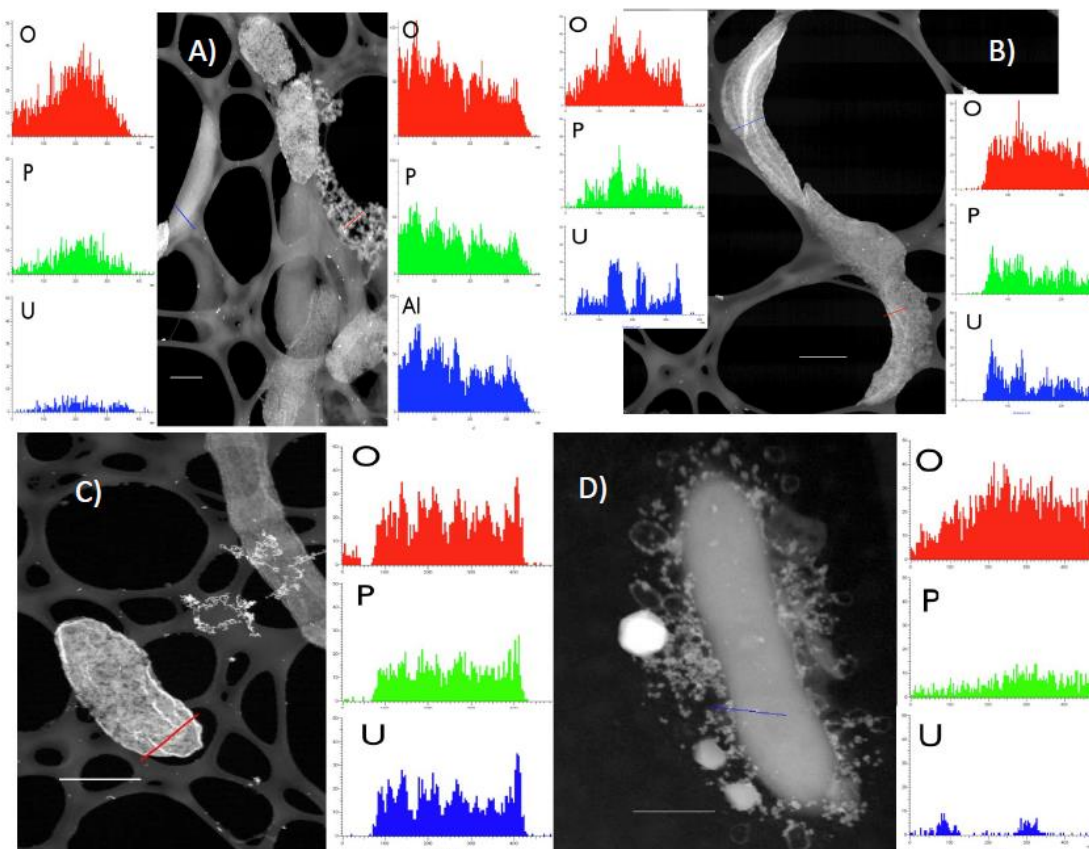


Figure 6: XEDS of (A and B) wild-type, (B)  $\Delta pilA$ , and (C)  $\Delta BESTZ$  respiring U(VI). High angle annular of dark field STEM images of areas of freeze-dried cryo-TEM grids. The “spider web-like” pattern supporting the cells is the lacey carbon support. The scattering from metal aggregates and gold beads appears intensely bright. The red and blue lines indicate the line scanned by the probe. Scale bar: 500 nm. Side panels show x-ray counts of the main elements along the scanned line. The units in the line scans are nm on the x-axis and x-ray counts on the y-axis. For O (oxygen), P (phosphorus) and Al (aluminum) it is the number of x-ray counts in their K alpha peaks, and for U it is the number of counts in the L alpha peak. Uranium counts are significantly above background.



## CHAPTER 3

### PROTEOME OF GEOBACTER SULFURREDUCTENS IN THE PRESENCE OF U(VI)

**3 Abstract** *Geobacter* species often play an important role in the *in situ* bioremediation of uranium-contaminated groundwater, but little is known about how these microbes avoid uranium toxicity. To evaluate this further, the proteome of *G. sulfurreducens* exposed to 100  $\mu$ M U(VI) acetate was compared with control cells not exposed to U(VI). Of the 1363 proteins detected from these cultures, 203 proteins had higher abundance during exposure to U(VI) compared to the control cells and 148 proteins had lower abundance. U(VI)-exposed cultures expressed lower levels of proteins involved in growth, protein and amino acid biosynthesis, as well as key central metabolism enzymes as a result of the deleterious effect of U(VI) in the growth of *G. sulfurreducens*. In contrast, proteins involved in detoxification, such as several efflux pumps belonging to the RND family, and protection of membrane and proteins, such as chaperons and proteins involved in secretion systems, were in higher abundance in cells exposed to U(VI). Exposing *G. sulfurreducens* to U(VI) resulted in higher abundance of many proteins associated with the oxidative stress response, such as superoxide dismutase and superoxide reductase. A strain in which the gene for superoxide dismutase was deleted grew slower than the wild-type strain in the presence U(VI), but not in its absence. The results suggest that there is not one specific mechanism for uranium detoxification. Rather, multiple general stress responses are induced, which presumably enable *Geobacter* species to tolerate high uranium concentrations.

#### 3.1 Introduction

Uranium contamination of sediments and ground/surface water has become a serious environmental concern, especially at many former uranium mining and processing facilities (4, 5, 66). One strategy for preventing the spread of uranium in the subsurface is to take advantage of the ability of some microorganisms to reduce soluble U(VI) to poorly soluble U(IV) (7, 12, 20, 30, 73, 75, 104). This approach has been investigated in a diversity of subsurface sites (2, 4, 105, 106). In many instances, stimulation of dissimilatory metal reduction with organic electron donors specifically enriches *Geobacter* species which are highly effective in U(VI) reduction (1, 2).

*Geobacter sulfurreducens* has served as the primary model organism to elucidate the physiological capabilities of *Geobacter* species (1, 107). Gene deletion and uraninite localization studies have suggested that *G. sulfurreducens* reduces U(VI) at the outer cell surface with a diversity of *c*-type cytochromes (3, 52). However, some uranium may enter the cell, and little is known about the physiological response to this uranium. Unlike essential metals that can be imported or extruded depending on requirements of the cell (108), uranium is not expected to be a required nutrient and is likely to be toxic because U(VI) can denature proteins, inactivate functional groups of enzymes, disrupt the cell envelope, and damage DNA (70, 72). There is not yet evidence for U(VI)-specific transport or a protective mechanism in any bacteria, suggesting that physiological systems designed for handling other toxic materials may also deal with U(VI) toxicity.

In this study we employed a genome-scale proteomic analysis and targeted gene deletions to gain insights into the impact of uranium exposure on the physiology of *G. sulfurreducens*. The results suggest that rather than a U(VI)-specific detoxification system, *G. sulfurreducens* utilizes a combination of mechanisms to cope with stress produced by U(VI).

### **3.2 Materials and Methods**

### 3.2.1 Strains and culturing

*Geobacter sulfurreducens* strain DL-1(32) as well as  $\Delta$ sodA (37),  $\Delta$ GSU2212 (109),  $\Delta$ GSU2213 (109),  $\Delta$ BESTZ (62) were obtained from our laboratory culture collection. Cells were routinely grown in anaerobic medium with acetate as the electron donor and fumarate as the electron acceptor (110).

For proteomic analysis of the impact of U(VI) exposure, 100  $\mu$ M U(VI)-acetate was added to mid-log phase cultures. Cells were collected by centrifugation at 9,000\*g for 15 min at 4°C, washed with 50mM Tris-HCl containing 10 mM MgCl<sub>2</sub> and protease inhibitors and stored at -20 °C until use. Controls received no U(VI) additions.

### 3.2.2 Protein Digestion and Desalting

For the global trypsin digestion the cells were re-suspended in 4 cell volumes of a denaturation solution of 7 M urea, 2 M thiourea and 5 mM DTT in 50 mM ammonium bicarbonate, pH 7.8. Cells were lysed by bead beating. The cells were mixed with 0.1 mm zirconia/silica beads in a mini-bead beater (Biospec, Bartlesville OK) for 90 s at 4500 rpm. Isolated proteins were diluted with a 10-fold volume of 50 mM ammonium bicarbonate, pH 7.8, CaCl<sub>2</sub> was added to a concentration of 2 mM, and trypsin was added in a w/w ratio of 1:50, trypsin:total protein. The proteins were digested with trypsin for 8 hours at 37 °C. The resulting peptides were desalted with a Supelclean C-18 column (Supelco, St. Louis MO) using a 5% acetonitrile in water wash buffer and an 80% acetonitrile in water elution buffer. The peptides were concentrated to dryness with a SpeedVac (ThermoSavant, Milford MA) and were reconstituted in ~100  $\mu$ L of nanopure water. Total peptide concentration was determined with the BCA assay (Pierce, Rockford IL). The peptides were quick frozen in liquid nitrogen and stored at -80°C until further analysis.

### 3.2.3 Tandem MS, MS and putative peptide identification

The capillary LC system consisted of a pair of syringe pumps (100-ml ISCO model 100DM) and controller (series D ISCO) and an in-house manufactured mixer, capillary column selector, and sample loop for manual injections. Separations were achieved with a 5,000 psi reversed-phase in-house packed capillary (150  $\mu\text{m}$  i.d.  $\times$  360  $\mu\text{m}$  o.d.; Polymicro Technologies, Phoenix) by using two mobile-phase solvents consisting of 0.2% acetic acid and 0.05% trifluoroacetic acid (TFA) in water (A) and 0.1% TFA in 90% acetonitrile/10% water (B). The mobile-phase selection valve was switched from position A to B 10 min after injection, creating an exponential gradient as mobile phase B displaced A in the mixer. Flow through the capillary HPLC column was  $\sim$ 1.8  $\mu\text{l}/\text{min}$  when equilibrated to 100% mobile-phase A.

Sample eluate from the HPLC was infused into a conventional ion trap MS (LCQ, ThermoFinnigan, San Jose, CA) operating in a data-dependent MS/MS mode over a 400 to 2000  $m/z$  range. For each cycle, the three most abundant ions from MS analysis were selected for MS/MS analysis by using a collision energy setting of 30%. Dynamic exclusion was used to discriminate against previously analyzed ions. The collision induced dissociation spectra from the conventional ion trap mass spectrometer were analyzed using SEQUEST (111) and the genome sequence of *Geobacter sulfurreducens* (112). Initial peptide identifications (i.e. putative mass and time tags: PMT tags) were based on a minimum cross correlation (Xcorr) score of 1.5 for all peptides identified at least twice in all MS/MS experiments. For peptides only identified once, Xcorr values had to be a minimum of 1.9, 2.2, and 3.5 for charge states of 1+, 2+ and 3+, respectively. All peptides conformed to a tryptic cleavage state on at least one of their termini.

Using the same LC conditions, each sample was further analyzed in triplicate by FTICR-MS. The FTICR mass spectrometers developed at our laboratory use ESI interfaced with an electrodynamic ion funnel assembly coupled to a radio frequency quadrupole for collisional ion focusing and highly efficient ion accumulation and transport to a cylindrical FTICR cell for analysis (113).

#### **3.2.4 Determination of Accurate Mass and Time (AMT) Tags**

The peptide library (containing peptide sequence information, elution time information and the theoretical mass) were then compared with the high resolution high accuracy peptide mass and elution time obtained from the FTICR MS runs. These peptides that were matched and verified in this manner were then deemed accurate mass and time (AMT) tags. More details as to AMT tag validation has been previously described (114). Briefly, the resultant FTICR data was processed using the PRISM Data Analysis system, a series of software tools developed in-house. The first step involved de-isotoping the MS data, giving the monoisotopic mass, charge, and intensity of the major peaks in each mass spectrum. Following this, the data was examined in a two-dimensional fashion to find the groups of mass spectral peaks that were observed in sequential spectra. Each group, known as a unique mass class (UMC), has a median mass, central normalized elution time (NET), and abundance estimate, computed by summing the intensities of the MS peaks that comprise the UMC.

The identity of the UMC's was determined by comparing the mass and NET of each UMC with the mass and NET's of all identified peptides ascertained from all prior MS/MS analyses performed on *G.sulfurreducens*. Search tolerances were  $\pm 6$  ppm for the mass and  $\pm 5\%$  of the total run time for the elution time. Relative abundance values for each peptide were determined from the summed ion current value of all MS scans that detected the peptide eluting. Protein values were represented by the most abundant peptide values observed for each protein.

The abundance values for each protein in each analysis were transformed into a z-score value (also known as the standard row function) to determine those showing significant changes from their average values. The z-score is obtained by using the mean value of each protein across all compared growth conditions, subtracted from each individual protein abundance value and divided by the standard deviation of the values. Generally, z-score values between samples were considered significantly different if the difference was at least 1.5 or greater.

### **3.2.5 Impact of mutations on growth in the presence of U(VI)**

We monitored the growth of the aforementioned strains under the two following conditions “environmental relevant stress” (in the presence of 100  $\mu$ M of U(VI) in the form of uranyl acetate) and “severe U(VI) stress” (in the presence of 1 mM of U(VI) in the form of uranyl acetate). Cells were grown in acetate-fumarate medium in anaerobic pressure tubes (32). Each culture was inoculated with 5% mid-log-phase cells. Uranium was added to a final concentration of 100  $\mu$ M and 1 mM from a concentrated stock of uranyl acetate (20 mM) dissolved in bicarbonate buffer. An equivalent volume of bicarbonate buffer (41 mM) was added to uranium-free control cultures. During incubation, culture tubes were shaken horizontally to minimize the attachment of cells on the glass. Cell numbers were determined with epifluorescence microscopy utilizing cells stained with acridine orange (0.01%) as previously described (115). In order to have a statistically relevant description of growth, over 8 fields were recorded for each time point in three independent replicate cultures. Images were taken digitally with the SimplePCI software, version 5.3 (C-Imaging Systems, Compix Inc., Mars, PA) and cells were quantified using ImageJ software (NIH, <http://rsb.info.nih.gov/ij/>).

### 3.3 Results

In order to evaluate how bacterial cells respond to the presence of U(VI), *G. sulfurreducens* three biological replicates were grown anaerobically to mid-log phase, exposed to 100  $\mu$ M uranyl acetate for four hours, and then harvested for proteomic analysis. A total of 1363 proteins were detected in cells from these cultures. This represented about 40% of the 3469 predicted protein-encoding open reading frames in the genome of *G. sulfurreducens* (83). There were 203 proteins detected with higher abundance during exposure to U(VI) compared to the control cells not exposed to U(VI) and 148 proteins with lower abundance (Tables B1 and B2). This accounted for 26% of the total proteins detected indicating that protein expression was significantly affected by the presence of U(VI).

Proteins with differential expression in the presence of U(VI) were classified under 17 categories according to their annotation function in the genome (Figure 7, Tables B3-

B19). Proteins associated with energy conservation (26) had the highest number of proteins with greater abundance following uranium exposure, other than proteins with unknown function and hypothetical proteins (58). The majority of proteins that were in lower abundance in the uranium-exposed cells were also annotated as hypothetical proteins (29), proteins of unknown function (24) and proteins involved in energy metabolism (20) (Figure 7; Tables B1 and B2).

### 3.3.1 Proteins involved in growth

Exposure to U(VI) slightly reduced the growth rate of *G. sulfurreducens* (Figure 8) and many proteins associated with the central metabolism were in lower abundance in cells exposed to U(VI). For example, the expression of citrate synthase (GltA, GSU1106), which is directly correlated with metabolic rates of *G. sulfurreducens* (76, 116, 117), was lower in the presence of U(VI) compared to the untreated control (Table 1), suggesting that metabolism was slower in the presence of U(VI). Phosphoenolpyruvate synthase (PpsA, GSU0803), another enzyme involved in the central metabolism (118), and two subunits of ATP synthase (GSU0108 and GSU0111) were also less abundant when U(VI) was present (Table 1).

It also appeared that protein biosynthesis was less important in the presence of U(VI), which was reflected in the lower abundance of proteins involved in translation, such as GSU1920 (elongation factor Ts), GSU0102 (selenocysteine-specific translation elongation factor), and GSU1516 (translation initiation factor IF-3); as well as several ribosomal proteins, such as RpsG, RplR, RpsT, YfiA, RplX, RpsS, RpsA, RplF, RpsK, and RpsP; and proteins involved in ribosome biogenesis, ObgE and EngB (Table 1). Proteins involved in amino acid biosynthesis, such as GSU1061 (aspartate aminotransferase), GSU3099 (histidinol-phosphate aminotransferase), GSU3095 (imidazole glycerol phosphate synthase subunit HisF), and GSU1828 (chorismate mutase) were also less abundant (Table 1).

### 3.3.2 Protein and DNA damage

Uranium has high affinity for organic molecules and can form strong bonds with functional groups in proteins (119). The uranium binding can produce conformational changes in proteins (120-122). Uranium ions can generate ligands with functional groups of thiolates as well as carboxylate from acidic amino acids, such as aspartate or glutamate (71, 122, 123). Enzymes in *G. sulfurreducens* that assist in protein folding may help to avoid these potential deleterious effects. For example, exposure to U(VI) resulted in higher expression of the chaperonin GroES (GSU3339), the DnaJ-related molecular chaperone (GSU0014) and the DnaJ adenine nucleotide exchange factor (GrpE, GSU0032) that is involved in the protection and renaturation of heat-labile proteins (Table 2).

The expression of several proteins related to peptide secretion and trafficking were also more abundant in the presence of U(VI). For example, the SecE and SecF (GSU2869 and GSU2616), which belong to the general Sec system, and PulQ (GSU1778) and GspK (GSU0322), which are part of the type II secretion system, were in higher abundance in the presence of U(VI) (Table 2). Previous studies have suggested that the type II secretion system has an essential role in localizing several metal-containing proteins on the outer surface of the cell (1, 112).

Uranium has a high affinity for DNA, which can result in DNA strand breakage and inhibits DNA-protein interactions (121, 123-125). Thus, the exposure to U(VI) could be expected to result in DNA damage. However, only three proteins involved in DNA metabolism, DnaA (GSU3470), TopA (GSU2549), and Ssb-2 (GSU3117), were more abundant following U(VI) exposure (Table 2), and surprisingly RecA (GSU0145), an essential protein for the repair and maintenance of DNA was in lower abundance in the presence of U(VI) (Table 1). This suggests that although some uranium was able to enter the cytoplasm, uranium scavenging enzymes were highly efficient, preventing the subsequent DNA damage.

### **3.3.3 Detoxification and Membrane damage**

Although there are no known uranium-specific detoxification systems in microorganisms, metal efflux pumps for other toxic metals exist (108) and could



conceivably play a role in preventing uranium toxicity. Several efflux pumps in the RND family, which confer metal tolerance by extruding a wide spectrum of metals, were more abundant in cells exposed to U(VI) (Table 2). For example, RND family proteins associated with the CzcABC complex, were triggered by the presence of U(VI). GSU2695 (RND-type efflux pump) and GSU1482 (CzcC, RND-type efflux pump), which correspond to outer membrane proteins able to transport heavy metals across the outer membrane, were more abundant in cells exposed to U(VI). The three membrane fusion proteins, GSU2136 (RND-type efflux pump), GSU2781 (RND-type efflux pump) and GSU0496 (RND-type efflux pump), which span the periplasmic space and funnel cations across it (126), were also in higher abundance in the presence of U(VI) (Table 2). Many other proteins related to binding and transport metals were also significantly more abundant in the presence of U(VI), such as the putative periplasmic tungstate ABC transporter (TupA, GSU2700) which is part of the tungstate transport complex and MgtA (GSU1678) commonly involved in  $Mg^{2+}$  transport (Table 2).

Another strategy for heavy metals detoxification is precipitation (4, 127, 128). Several microorganisms are known to use phosphate derived from polyphosphate to precipitate uranium (129). The polyphosphate kinase (Ppk-2, GSU0728), which catalyzes the transfer of phosphate from ATP to form a long-chain polyphosphate, and the exopolyphosphatase (GSU2559), which irreversibly hydrolyzes polyP to form phosphates, were both more abundant in cells exposed to uranium, suggesting a potential role in uranium detoxification (Table 2).

The lipid bilayer of the outer membrane is the most external barrier before the peptidoglycan in *G. sulfurreducens*. This layer is rich in phosphate and carboxylate groups, which may strongly bind U(VI) (129). Many lipoproteins such as GSU1817 (outer membrane lipoprotein, Slp family), GSU0457 (outer membrane lipoprotein LolB) and GSU0157 (lipoprotein) were more abundant in the presence of U(VI). A similar response was observed with proteins involved in peptidoglycan and cell wall biosynthesis, such as Ddl (GSU3066) and MurI (GSU2923), respectively (Table 2).

### **3.3.4 Proteins involved in oxidative stress**

*G. sulfurreducens* is an aerotolerant anaerobe, with effective mechanisms for dealing with oxidative stress (71, 130). Many proteins that are involved in the typical oxidative stress response in bacteria are also induced in response to other environmental stimuli, such as heat (131, 132), high salt concentrations (133) and heavy metals stress (131, 133-135). A number of proteins associated with the oxidative stress response were more abundant in cells exposed to uranium (Table 2). A possible explanation for this is that glutathione can reduce U(VI) that enters the cells, producing oxidized bisglutathione and hydrogen peroxide (67, 136, 137). This reduction could potentially be catalyzed by two proteins encoding typical 2-Cys subfamily of peroxiredoxins, GSU0352 and GSU3246, and glutaredoxin (GSU1155), which were more highly expressed in cells grown in the presence of U(VI) (Table 2). Homologs of rhodanese-like proteins (GSU0505 and GSU2516) that are involved in the oxidative stress response of *E. coli* (138), were also expressed in higher abundance when U(VI) was present (Table 2). Exposing *G. sulfurreducens* to U(VI) resulted in higher abundance of both superoxide dismutase (SodA, GSU1158) and superoxide reductase (GSU0720) (Table 2). A former transcriptional study of the *Geobacter* species that predominated during *in situ* uranium bioremediation at a field study site in Rifle, CO, reported that the gene encoding the superoxide dismutase (SodA) was highly expressed despite the presence of a highly reduced environment (139). Another study that evaluated the transcriptional expression of the *G. uraniireducens*, an isolate from the site (140), also found that the *sodA* gene was upregulated when the isolate was grown in the contaminated subsurface sediments (104). Both results suggested that the expression of SodA could not only be triggered as a result of oxygen stress, but also other factors in the sediments. Furthermore, the gene encoding the superoxide dismutase was upregulated when cells of the highly uranium tolerant oligotroph, *Caulobacter crescentus*, were exposed to uranium, cadmium, chromate, and dichromate (131), suggesting that this enzyme is involved in the response to a wide range of heavy metals.

In order to evaluate the role of superoxide dismutase in response to U(VI) stress, the growth of a SodA-deficient strain in the presence U(VI) was evaluated (Figure 9). In the absence of U(VI) the growth of the SodA-deficient strain was comparable to that of wild-type (Figure 8). However, in the presence of 100  $\mu$ M U(VI) the SodA-deficient

strain grew slower than wild-type (Figure 8). The impact of the loss of SodA was even more apparent in the presence of 1 mM U(VI) (Figure 9).

### 3.3.5 Extracellular matrix proteins

Two regulatory proteins (GSU2212 and GSU2213) related to the *che5* gene cluster, which has been shown to participate in the synthesis of extracellular matrix and biofilm formation (109), were more abundant in cells exposed to uranium (Table 2). In order to evaluate the potential role of these proteins in response to uranium toxicity cultures in which one of the genes for these proteins was deleted were grown in the presence of uranium (Figure 10 and 11). However, deletion of these genes did not significantly inhibit growth in the presence of uranium, suggesting that these regulatory proteins were not essential for the response to uranium toxicity.

### 3.3.6 *c*-type cytochromes

Three *c*-type cytochromes (GSU0357, GSU1648, and GSU2801) were expressed with higher abundance when cells were exposed to U(VI) (Table 2). GSU0357 is predicted to be a nitrite reductase. The function of GSU2801 is unknown. GSU2801 is not essential for Fe(III) oxide reduction in *G.sulfurreducens* (84), but, its homolog in *G. metallireducens* had higher transcript abundance in cells grown on Fe(III) oxide than in Fe(III) citrate-grown cells (84). GSU 1648 (*macC*) is predicted to be periplasmic. The gene encoding a *macC* homolog was more highly expressed in *G. uranireducens* grown in a U(VI)-contaminated subsurface than in culture medium (104).

A number of *G. sulfurreducens* outer-surface cytochromes appear to contribute to U(VI) reduction (3, 52). The reduction of U(VI) at the outer surface might be expected to be one mechanism for reducing uranium toxicity because poorly soluble U(IV) is unlikely to enter the cell. To test this concept, studies were conducted with the previously described quintuple mutant (62) in which the genes for the outer-surface *c*-type cytochromes OmcB, OmcE, OmcS, OmcT, and OmcZ were deleted. Although cell suspensions of this quintuple mutant reduced U(VI) at a rate only 18 % that of wild-type

cells (Orellana *et al.*, 2013), this strain grew as well as the wild-type strain in the presence of U(VI) (Figure 1).

### **3.4 Implications**

The ability of *G. sulfurreducens* (this study) and other *Geobacter* species (20) to grow in the presence of mM quantities of uranium is remarkable because it is unlikely that there has ever been any major evolutionary pressure on these organisms to deal with such high concentrations of uranium in natural environments. The differential expression of proteins in the presence of U(VI) did not reveal a specific U(VI)-detoxification system. Rather, resistance to U(VI) appears to be accomplished with multiple stress response systems and regulatory networks that facilitate fast adaptation to rapidly changing conditions. The ability of *Geobacter* species to cope with potential U(VI) toxicity in this manner may be one of the reasons that *Geobacter* species are often one of the most abundant genera of microorganisms during *in situ* uranium bioremediation.

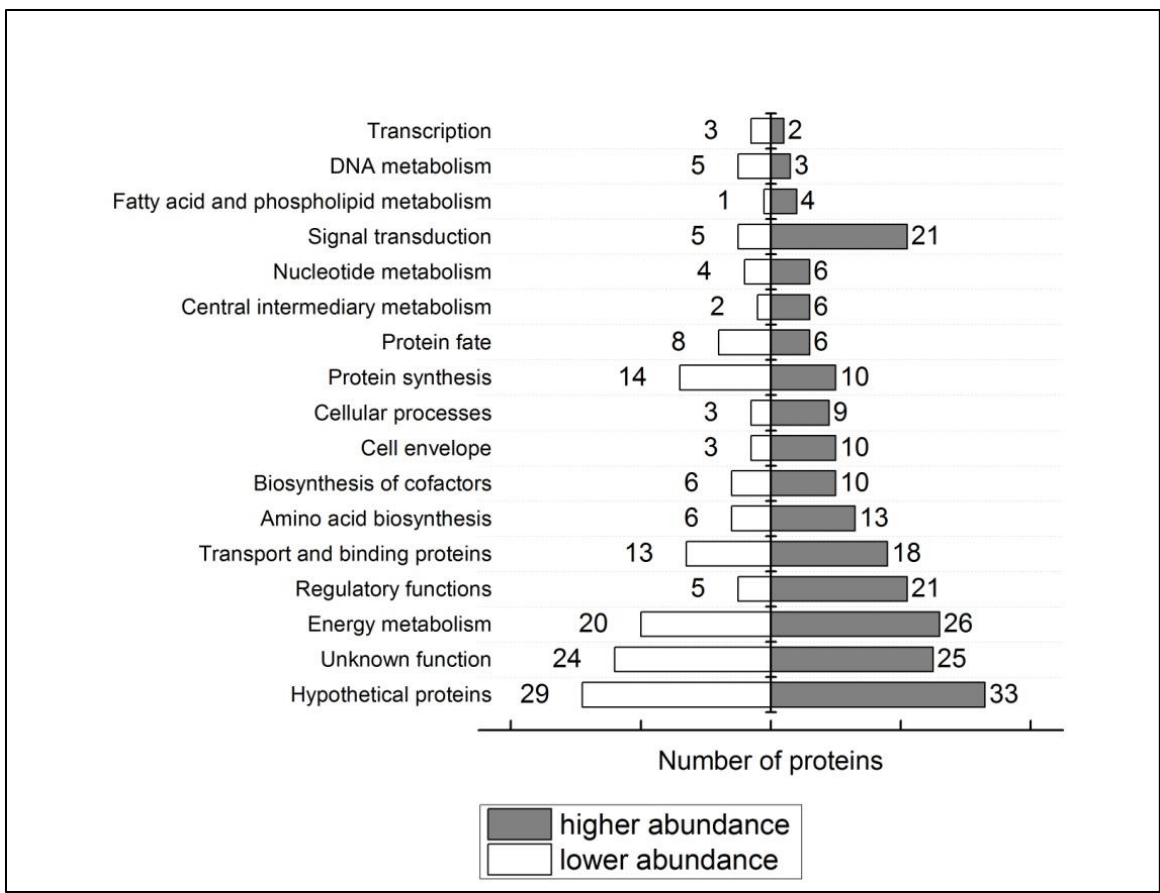


Figure 7: Changes in the protein profile as a result of U(VI) exposure. In the right side, number of proteins with increased relative abundance. In the left side, number of proteins with lower relative abundance. The proteins are grouped according to functional class as defined by the TIGR annotation.

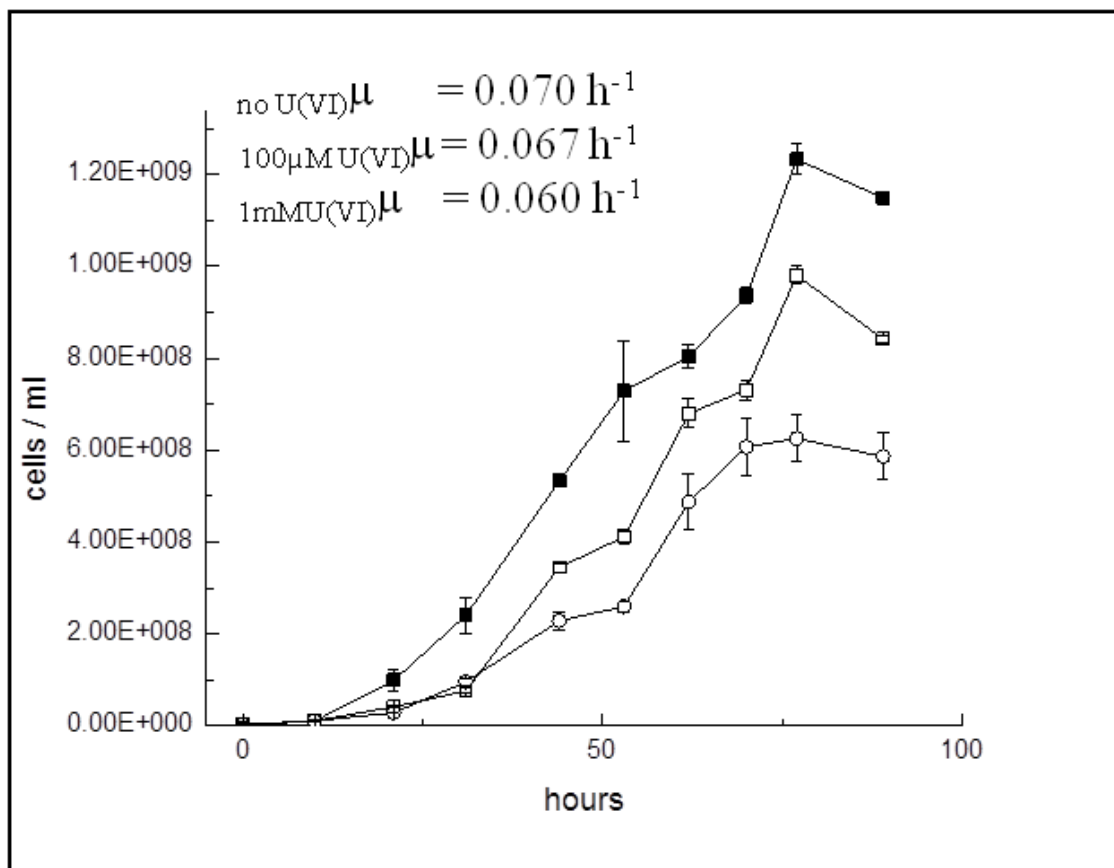


Figure 8: Effect of U(VI) on the growth of wild-type. Solid boxes indicate cultures grown in absence of U(VI). Empty boxes indicate cultures grown in the presence of 100 μM of U(VI). Each point in the curve is the mean from three independent replicate cultures. Bars designate one standard deviation of the mean.

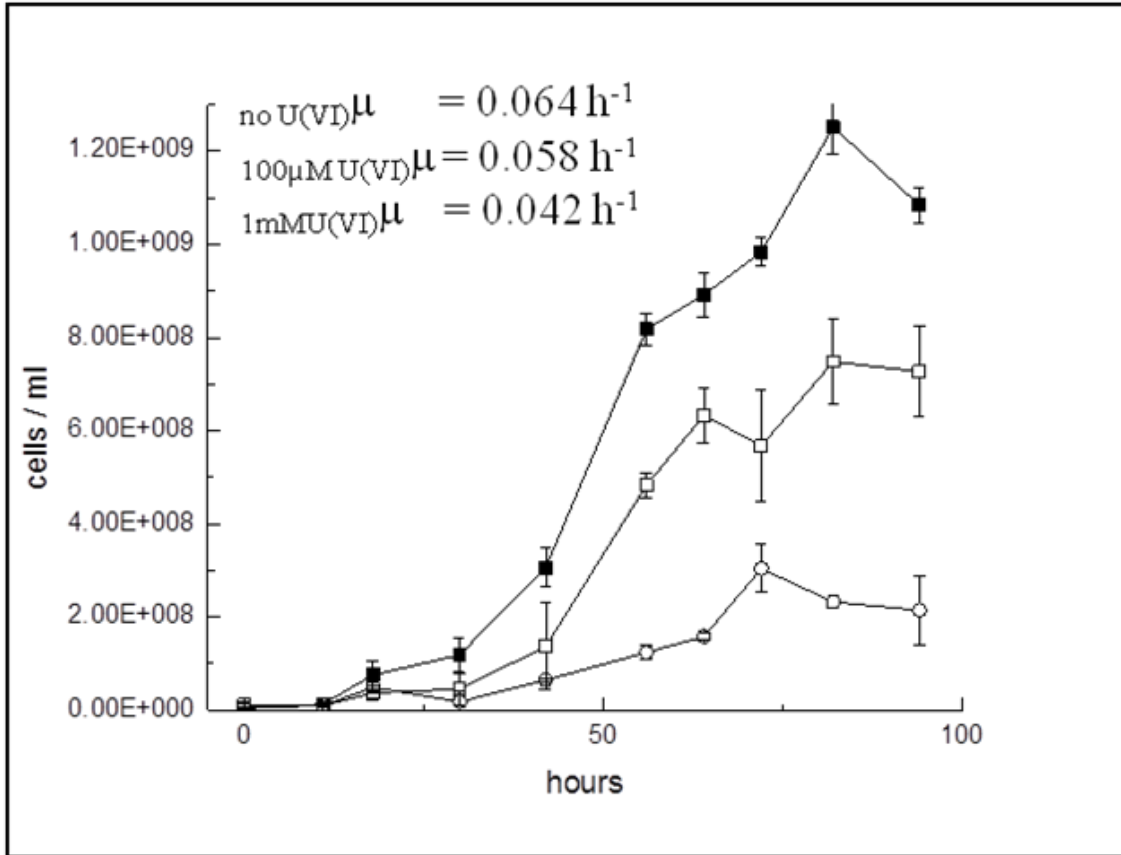


Figure 9: Effect of U(VI) on the growth of  $\Delta\text{sodA}$ . Solid boxes indicate cultures grown in absence of U(VI). Empty boxes indicate cultures grown in the presence of 100  $\mu\text{M}$  of U(VI). Each point in the curve is the mean from three independent replicate cultures. Bars designate one standard deviation of the mean.

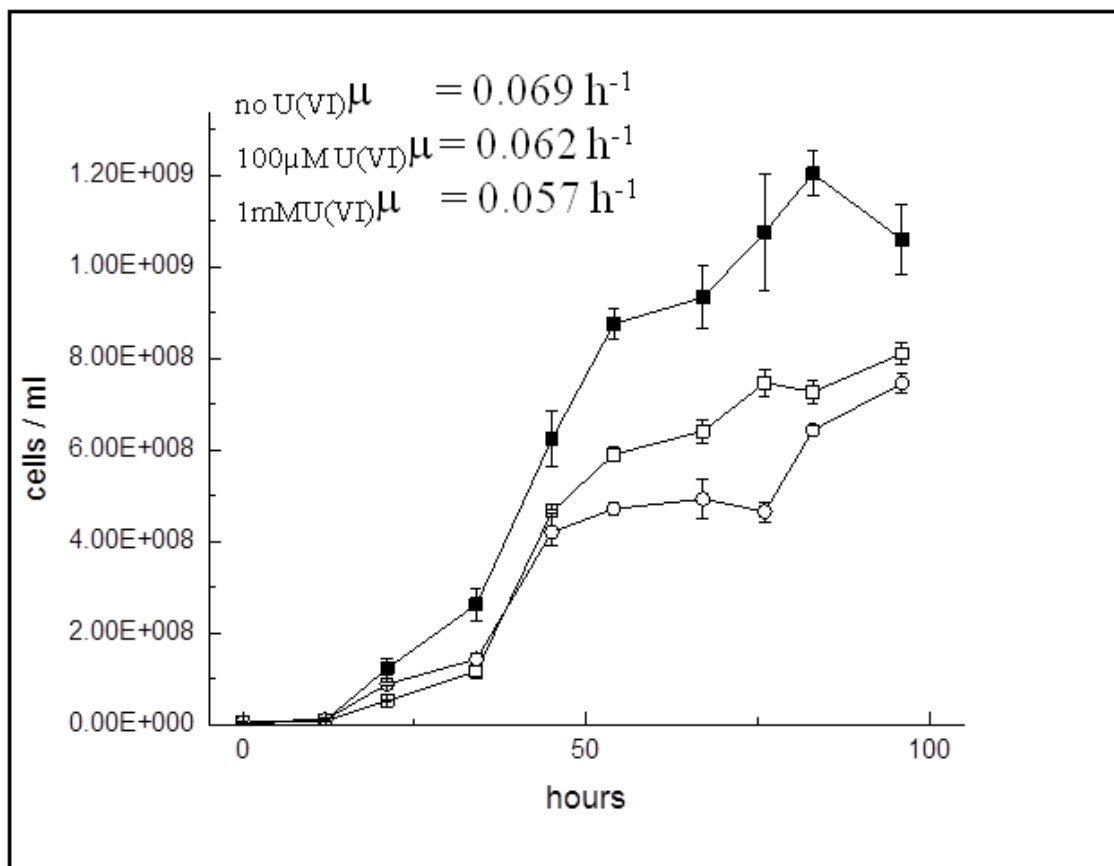


Figure 10: Effect of U(VI) on the growth of  $\Delta$ GSU2212. Solid boxes indicate cultures grown in absence of U(VI). Empty boxes indicate cultures grown in the presence of 100  $\mu\text{M}$  of U(VI). Each point in the curve is the mean from three independent replicate cultures. Bars designate one standard deviation of the mean.



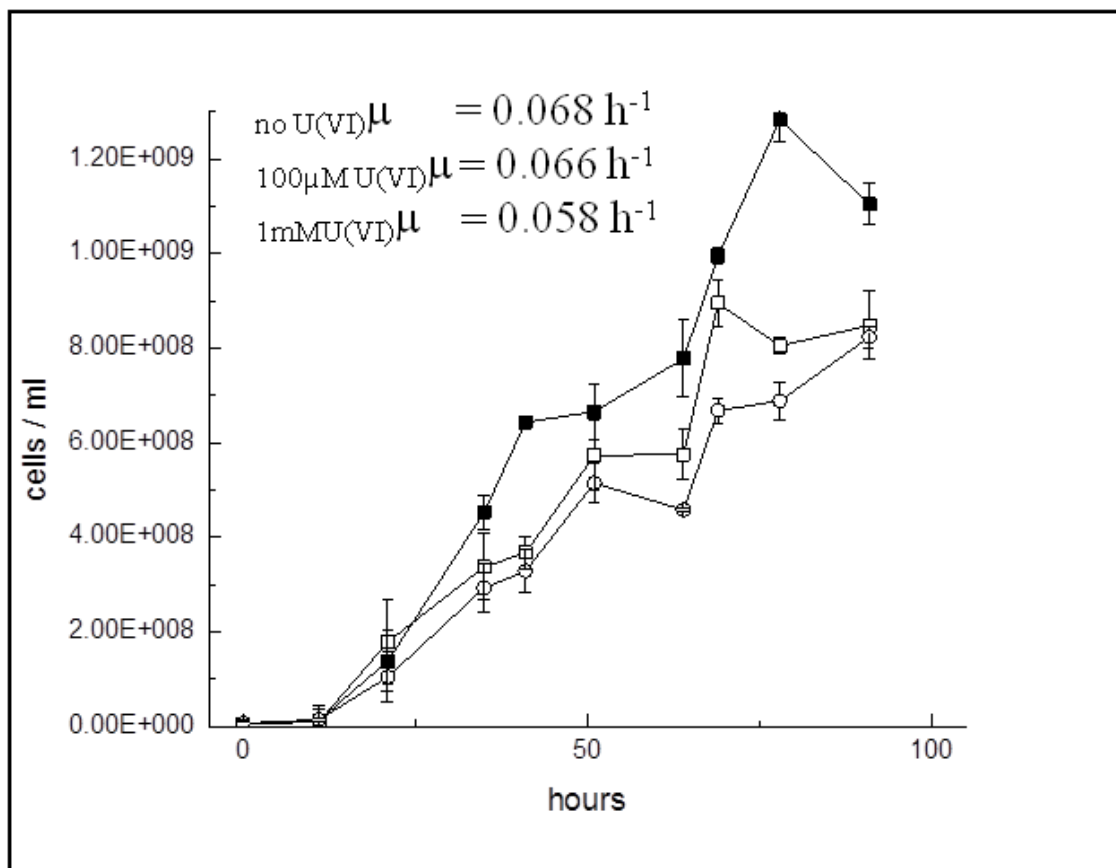


Figure 11: Effect of U(VI) on the growth of  $\Delta$ GSU2213. Solid boxes indicate cultures grown in absence of U(VI). Empty boxes indicate cultures grown in the presence of 100  $\mu$ M of U(VI). Each point in the curve is the mean from three independent replicate cultures. Bars designate one standard deviation of the mean.

Table 1: Selected proteins with lower relative abundance during exposure to U(VI) compared to the control cells. The right column indicates the z-score (also called the Standard Row Function). z-score were obtained by using the mean value of each protein across both conditions, subtracted from each individual protein abundance value and divided by the standard deviation of the values. z-score values between samples were considered significantly different if the difference was at least 1.5 or greater.

| Locus ID  | Gene Annotation                                       | Gene name | z- score difference<br>( $Z_{U(VI)} - Z_{control}$ ) |
|---|---|-----------|--|
| <b>Proteins involved in growth</b>                |   |           |  |
| <i>Central metabolism and energy conservation</i> |   |           |  |
| GSU1106   | citrate synthase                                      | gltA      | -1.65  |
| GSU0803   | phosphoenolpyruvate synthase                          | ppsA      | -1.62  |
| GSU0108   | ATP synthase F0, B subunit, putative                  |           | -1.59  |
| GSU0111   | ATP synthase F1, alpha subunit                        | atpA      | -1.74  |
| <i>Translation and protein synthesis</i>          |   |           |  |
| GSU1920   | translation elongation factor Ts                      | tsf       | -1.65  |
| GSU0102   | selenocysteine-specific translation elongation factor | selB      | -1.70  |
| GSU1516   | translation initiation factor IF-3                    | infC      | -1.51  |
| GSU2861   | ribosomal protein S7                                  | rpsG      | -1.51  |
| GSU2841   | ribosomal protein L18                                 | rplR      | -1.53  |
| GSU2206   | ribosomal protein S20                                 | rpsT      | -1.54  |
| GSU1886   | ribosomal subunit interface-associated sigma-54       | yfiA      | -1.55  |

|                                |  |      |       |
|--------------------------------|--|------|-------|
|                                | modulation protein                                     |      |       |
| GSU2846                        | ribosomal protein L24                                  | rplX | -1.57 |
| GSU2853                        | ribosomal protein S19                                  | rpsS | -1.57 |
| GSU2603                        | ribosomal protein S1                                   | rpsA | -1.67 |
| GSU2842                        | ribosomal protein L6                                   | rplF | -1.69 |
| GSU2833                        | ribosomal protein S11                                  | rpsK | -1.72 |
| GSU0643                        | ribosomal protein S16                                  | rpsP | -1.73 |
| <i>Ribosome biogenesis</i>     |  |      |       |
| GSU3213                        | ribosome biogenesis GTPase ObgE                        | obgE | -1.74 |
| GSU3013                        | GTPase EngB  | engB | -1.79 |
| <i>Amino acid biosynthesis</i> |  |      |       |
| GSU1061                        | aspartate aminotransferase                             |      | -1.53 |
| GSU3099                        | histidinol-phosphate aminotransferase                  | hisC | -1.63 |
| GSU3095                        | Imidazole glycerol phosphate synthase, cyclase subunit | hisF | -1.64 |
| GSU1828                        | chorismate mutase                                      |      | -1.66 |
| <b>DNA repair</b>              |  |      |       |
| GSU0145                        | recA protein   | recA | -1.60 |

Table 2: Selected proteins with higher relative abundance during exposure to U(VI) compared to the control cells. The right column indicates the z-score (also called the Standard Row Function). z-score were obtained by using the mean value of each protein across both conditions, subtracted from each individual protein abundance value and divided by the standard deviation of the values. z-score values between samples were considered significantly different if the difference was at least 1.5 or greater.

| Locus ID                                 | Gene Annotation                                    | Gene name | z- score difference<br>( $z_{U(VI)} - z_{control}$ ) |
|--|--|-----------|--|
| <b>Protein and DNA damage</b>            |  |           |  |
| <i>Protein folding</i>                   |  |           |  |
| GSU3339                                  | chaperonin GroES                                   | groES     | 1.54   |
| GSU0014                                  | DnaJ-related molecular chaperone                   |           | 1.82   |
| GSU0032                                  | DnaJ adenine nucleotide exchange factor GrpE       | grpE      | 1.63   |
| <i>Peptide secretion and trafficking</i> |  |           |  |
| GSU2869                                  | preprotein translocase, SecE subunit               | secE      | 1.73   |
| GSU2616                                  | protein-export membrane protein SecF               | secF      | 1.50   |
| GSU1778                                  | type II secretion system secretin lipoprotein PulQ | pulQ      | 1.65   |
| GSU0322                                  | type II secretion system protein GspK              | gspK      | 1.54   |
| <i>DNA protection</i>                    |  |           |  |
| GSU3470                                  | chromosomal replication initiator protein DnaA     | dnaA      | 1.78   |
| GSU2549                                  | DNA topoisomerase I                                | topA      | 1.68   |
| GSU3117                                  | single-strand binding protein                      | ssb-2     | 1.67   |

| <b>Detoxification and membrane damage</b>       |  |       |      |
|---|--|-------|------|
| <i>Detoxification</i>                           |  |       |      |
| GSU2695   | efflux pump, RND family, outer membrane protein                            |       | 1.77 |
| GSU1482   | efflux pump, RND family, outer membrane protein                            |       | 1.81 |
| GSU2136   | efflux pump, RND family, membrane fusion protein                           |       | 1.71 |
| GSU2781   | efflux transporter, RND family, MFP subunit                                |       | 1.64 |
| GSU0496   | efflux transporter, RND family, MFP subunit                                |       | 1.56 |
| GSU2700   | tungstate ABC transporter, periplasmic tungstate-binding protein, putative | tupA  | 1.77 |
| GSU1678   | cation-transport ATPase, E1-E2 family                                      | mgtA  | 1.54 |
| <i>Polyphosphate metabolism</i>                 |  |       |      |
| GSU0728   | polyphosphate kinase   | ppk-2 | 1.55 |
| GSU2559   | Exopolyphosphatase   |       | 1.64 |
| <i>Lipoproteins</i>                             |  |       |      |
| GSU1817   | outer membrane lipoprotein, Slp family                                     |       | 1.79 |
| GSU0457   | outer membrane lipoprotein LolB, putative                                  |       | 1.76 |
| GSU0157   | lipoprotein, putative  |       | 1.65 |
| <i>Peptidoglycan and cell wall biosynthesis</i> |  |       |      |
| GSU3066   | D-alanine--D-alanine ligase  | ddl   | 1.74 |

|  |   |        |      |
|--|---|--------|------|
| GSU2923                                  | glutamate racemase                            | murI   | 1.66 |
| <b>Oxidative stress response</b>         |   |        |      |
| <i>Peroxiredoxins and glutaredoxins</i>  |   |        |      |
| GSU0352                                  | peroxiredoxin, atypical 2-Cys subfamily       | prx-3  | 1.66 |
| GSU3246                                  | peroxiredoxin, typical 2-Cys subfamily        | prx-2  | 1.80 |
| GSU1155                                  | glutaredoxin family protein                   |        | 1.77 |
| <i>Rhodanase like proteins</i>           |   |        |      |
| GSU0505                                  | rhodanese homology domain superfamily protein |        | 1.66 |
| GSU2516                                  | rhodanese homology domain pair protein        |        | 1.77 |
| <i>Reduction/oxidation of superoxide</i> |   |        |      |
| GSU0720                                  | superoxide reductase                          |        | 1.78 |
| GSU1158                                  | superoxide dismutase                          | sodA   | 1.72 |
| <b>Extracellular matrix proteins</b>     |   |        |      |
| <i>Chemotaxis</i>                        |   |        |      |
| GSU2212                                  | chemotaxis protein CheY                       | cheY-5 | 1.71 |
| GSU2213                                  | GAF domain protein                            |        | 1.82 |
| <b>c-type cytochromes</b>                |   |        |      |
| <i>Periplasmic cytochromes</i>           |   |        |      |
| GSU0357                                  | cytochrome c family protein                   |        | 1.74 |
| GSU2801                                  | cytochrome c, 5 heme-binding sites            |        | 1.72 |
| GSU1648                                  | cytochrome c, 5 heme-binding sites            | macC   | 1.73 |

## CHAPTER 4

### NOVEL MEMBRANE-BOUND COMPLEXES INVOLVED IN ENERGY CONSERVATION BY THE ACETATE OXIDIZING SULFATE-REDUCING BACTERIUM *DESULFOBACTER POSTGATEI*

#### 4 Abstract

*Desulfobacter postgatei* is a pure culture model for the *Desulfobacter* species that plays an important role in sulfate reduction in marine sediments and that have a negative impact on *in situ* uranium bioremediation by outcompeting U(VI)-reducing species for acetate. In order to learn more about the mechanisms by which *D. postgatei* conserves energy from acetate oxidation couple to sulfate reduction, the genome of *D. postgatei* was sequenced and a genome-scale metabolic model was constructed. The model was improved and validated through several iterations of hypothesis generation. The integration of these predictions with bibliographic and experimental data based on continuous-culture system, allowed us to describe novel elements for energy conservation in *D. postgatei*. These included the energy-converting hydrogenase related complex, Ehr, the quinone-reductase complex, Qrc, the proton-translocating ferredoxin:NADP<sup>+</sup> oxidoreductase, Rnf, and also the NADH-dependent ferredoxin:NADP<sup>+</sup> oxidoreductase, Nfn. The current version of the model predicts that these complexes actively regulate the transition of the cells into different physiological states, providing also a link between the ferredoxin and NAD(H)/NADP(H) pools. RNA-seq analysis of transcript abundance in cells grown in an acetate-limited chemostat at different growth rates (0.014–0.032 h<sup>-1</sup>) revealed that many of the genes encoding proteins involved in these complexes were expressed in higher abundance as respiration rates increased. This new understanding of *D. postgatei* energy conservation will substantially improve the modeling of the growth of this organism in marine sediments and subsurface environments and also highlight how genome-scale metabolic modeling, coupled with enhanced genome annotation and experimental studies, can accelerate the study of the physiology of environmentally relevant, but understudied microorganisms.

## 4.1 Introduction

Sulfate-reducing bacteria (SRB) are a phylogenetically and physiologically diverse group of microorganisms that have in common the use of sulfate as an electron acceptor, which results in the production of sulfide as the end-product (141). SRB are anaerobic microorganisms that are ubiquitous in many anoxic environments where sulfate is available and they represent one of the more ancient metabolic processes (142). These organisms can use several fermentation products as electron donors, including hydrogen and organic compounds such as acetate, ethanol, formate, lactate, pyruvate, malate and succinate (143, 144).

SRB can be divided in two major physiological groups, the ones that incompletely degrade organic compounds to acetate and the ones that completely degrade organic compounds to CO<sub>2</sub> (143). Complete acetate oxidation is an ecophysiological relevant metabolic trait due to the fact that acetate is the most important intermediate in anoxic sediments in which sulfate reduction is the predominant terminal electron-accepting process, such as many marine environments and fresh water sediments with high concentration of sulfate (145-149). The high mineralization observed in those environments, especially in marine sediments with high input of organic matter, is linked to the activity of acetate-oxidizing SRB (150). Indeed, previous evidence has shown that more than 50% of the mineralization of organic carbon is metabolized by sulfate-reducing organisms suggesting that the activity of acetate-oxidizing SRB is central to today's biogeochemical cycling of carbon and sulfur (142, 145).

There are few SRB isolates that are capable of acetate oxidation. Among them, *Desulfobacter postgatei* is the only with a genome sequence available one that uses a modified citric acid cycle. *D. postgatei* strain 2ac9 is a Gram-negative, acetate-oxidizing SRB that was isolated from a brackish water ditch near Jadebusen (North Sea) (151). Acetate is used as both electron-donor and carbon source (152, 153). It can use other electron acceptors other than sulfate for growth including sulfite, thiosulfate and chelated Fe(III) (26). Described as a specialist due to its narrow capabilities to use substrates, *D. postgatei* has been shown to be a good scavenger of acetate. Therefore, it is expected that



this bacterium is widespread in environments limited by carbon availability (154).

Despite the importance of acetate-oxidizing SRB in sulfur and carbon cycles, investigations of their metabolism are scarce. A large part of the present knowledge of sulfate reduction metabolism has been derived from experiments with species belonging to the *Desulfovibrio* genus because a genetic system is available (155-158). In these studies, novel soluble and membrane-bound complexes involved in energy conservation have been recently discovered (155, 159-166), emphasizing our current lack of understanding about the metabolism of SRB. Furthermore, this is augmented by the fact that some of these enzymes might vary in function or directionality under different conditions (156).

Constraint-based modeling is an approach for quantitative prediction of the behavior of complex biological systems and their responses to the environment. To date, this method has been successfully applied to provide physiological and ecological insights on the metabolism of many environmental relevant anaerobic bacteria (118, 167-169) and has been used to optimize its applications in energy production and bioremediation (44, 170). In this work, we applied a systems biology approach to study energy conservation mechanisms of *D. postgatei*. Initially the genome was sequenced and manually annotated, and a genome-scale metabolic model was developed. Then, through validation using chemostat-based experiments and genome-wide transcription analysis, we analyzed the metabolism of *D. postgatei*. Both metabolic predictions and RNA-seq analysis of transcript abundance revealed that novel elements described are involved in energy conservation. These included the energy-converting hydrogenase related complex, Ehr, the proton-translocating ferredoxin:NADP<sup>+</sup> oxidoreductase, Rnf, the quinone-reductase complex, Qrc, and also the NADH-dependent reduced ferredoxin:NADP<sup>+</sup> oxidoreductase, Nfn. This new understanding of *D. postgatei* energy conservation will substantially improve the modeling of the growth of this organism in marine sediments and subsurface environments.

## 4.2 Materials and methods

### 4.2.1 Organism

*Desulfobacter postgatei* strain Dangast 2ac9 (DSMZ 2034) was obtained from the German Collection of Microorganisms and Cell Cultures (Deutsche Sammlung von Mikroorganismen und Zellkulturen, DSMZ), Braunschweig, Germany.

### 4.2.2 Media and cultivation

*D. postgatei* was grown anaerobically under N<sub>2</sub>/CO<sub>2</sub> gas phase as originally described by Widdel and Pfenning (1981) (151) in mineral media supplemented with trace element solution SL10 (171) and vitamin solution (172). Mineral media was reduced with sulfide and bicarbonate was used as buffer. Cultivation was carried out at 30°C. Cultures were grown with 21 mM sodium acetate as the sole source of organic carbon and energy and sodium sulfate (20 mM) as the electron acceptor.

### 4.2.3 Chemostat experiments

*D. postgatei* was grown at 30°C in duplicated chemostats in 1-L glass vessels with a 900 ml working volume, within a water bath for temperature control. The culture vessel and all associated tubing were sterilized by autoclaving. The connections between tubes were made with stainless steel Luer fittings (Cole Palmer) and the culture was sampled through a steel canula connected to a stainless steel port. The medium was introduced into the culture vessel at a steady rate with a variable-speed dispensing pump (ISMATEC) and calibrated tubing (PharMed; 1.30 mm internal diameter). The culture media were constantly gassed (50 ml min<sup>-1</sup>) with a certified mixture of N<sub>2</sub>-CO<sub>2</sub> (80:20) passed through heated copper filings to remove any traces of oxygen. The culture exited vertically through a stainless steel canula, pushed by the gas overpressure in the headspace and is collected in the effluent reservoir. The culture was stirred at a constant speed of 600 r.p.m. with a magnetic bar. Steady-state cell growth was obtained after 3

volume refills and was confirmed by a constant cell density and concentrations of acetate and sulfate.

#### **4.2.4 Analytical methods**

Protein concentrations were determined as previously described (173). Sulfate concentrations were determined by ion chromatography (174) and fatty acid concentrations by high-pressure liquid chromatography (175). Sulfite concentrations were determined by colorimetry (176). Acetate consumption for cell mass synthesis was calculated according to the equation described before (177).  $K_s$  (half saturation constant) was calculated with the Lineweaver-Burk linearization method based on nutrient-limited chemostats (178, 179).

#### **4.2.5 DNA extraction and genome sequencing**

DNA for sequencing was extracted using the DNA Isolation Bacterial Protocol available through the JGI (<http://www.jgi.doe.gov>). The quality of DNA extracted was assessed by gel electrophoresis and NanoDrop (ThermoScientific, Wilmington, DE) according to the JGI recommendations, and the quantity was measured using the Quant-iT™ Picogreen assay kit (Invitrogen, Carlsbad, CA) as directed.

The draft genome of *D. postgatei* was generated at the Joint Genome Institute (JGI) using a combination of Sanger and 454 sequencing platforms. All general aspects of library construction and sequencing can be found at <http://www.jgi.doe.gov/>. 454 Pyrosequencing reads were assembled using the Newbler assembler version 1.1.02.15 (Roche). Large Newbler contigs were broken into 2,525 overlapping fragments of 1,000 bp and entered into assembly as pseudo-reads. The sequences were assigned quality scores based on Newbler consensus  $q$ -scores with modifications to account for overlap redundancy and to adjust inflated  $q$ -scores. A hybrid 454/Sanger assembly was made using the phrap assembler. Possible mis-assemblies were corrected with Dupfinisher or transposon bombing of bridging clones (180). Gaps between contigs were closed by

editing in Consed, custom primer walk or PCR amplification. The error rate of the completed genome sequence is less than 1 in 100,000.

#### **4.2.6 Genome annotation**

Genes were identified using a combination of Critica (181) and Glimmer (182) as part of the genome annotation pipeline at Oak Ridge National Laboratory (ORNL), Oak Ridge, Tennessee, USA, followed by a round of manual curation. The predicted CDSs were translated and used to search the National Center for Biotechnology Information (NCBI) nonredundant database (<http://www.ncbi.nlm.nih.gov/genome/3293>), UniProt, TIGRFam, Pfam, PRIAM, KEGG, COG, and InterPro databases. The tRNAScanSE tool (183) was used to find tRNA genes, whereas ribosomal RNAs were found by using BLASTn against the ribosomal RNA databases. The RNA components of the protein secretion complex and the RNaseP were identified by searching the genome for the corresponding Rfam profiles using INFERNAL (139). Additional gene prediction analysis and manual functional annotation was performed within the Integrated Microbial Genomes (IMG) platform (<http://img.jgi.doe.gov/>) developed by the Joint Genome Institute, Walnut Creek, California, USA (184).

#### **4.2.7 Metabolic Network Reconstruction**

The initial *D. postgatei* metabolic network was done by the combination of the rapid annotation using subsystem technology (RAST) server [33] and Model SEED pipeline [34]. Refinement of the draft metabolic network was completed with the help of several public databases, including KEGG [35], MetaCyc [36], UniProt [37], BRENDA [38], and TCDB [39]. New assigned open reading frames (ORFs) obtained from RAST annotation in the reconstruction were identified by known physiological features of *D. postgatei* or a local sequence similarity search (BLASTp) [37]. The reactions and genes in the draft model were manually reviewed using the gene annotations and the available biochemical and physiological information. The main features of the metabolism of *D. postgatei* are explained in Appendix C (Table C1).

The resulting network was then subjected to the gap filling process to allow biomass formation under physiological growth conditions. For gap filling, simulations were performed to determine if the networks could synthesize every biomass component and the missing reactions in the pathways were identified as previously described (185). These reactions were reviewed for gene association, or added as non-gene associated reactions to enable the formation of biomass by the reconstructed network.

Biomass compositions in the published *Geobacter sulfurreducens* (118) and *Rhodospirillum rubrum* (169) model were used as a model to create the biomass demand reactions in the initial *D. postgatei* metabolic network. Experiments were carried out to determine the biomass composition (dry basis) of 1 gram of *D. postgatei* cells (Tables C3 to C14). Cultures were grown to a final optical density at 600 nm (OD<sub>600</sub>) of 0.2 to measure DNA, RNA, protein, lipid, and carbohydrate content and dry cell weight. For the dry cell weight, five independent cell pellets from a 500-ml culture samples were resuspended in water and carefully transferred into pre-weighed Eppendorf microcentrifuge tubes, and then dried at 85°C until at least 3 days. The dry weight was measured on a balance with 0.1-mg accuracy (Mettler Toledo; PL303) (Table C3). For the macromolecular composition analysis, the amounts of protein, lipids and carbohydrates were determined by the bicinchoninic acid method (173), the sulfo-phospho-vanillin method (186) and colorimetric analysis (187), respectively (Table C4). DNA content was calculated following methodology explained before (188). RNA content was assumed to be an average between reported values for *G.sulfurreducens* (118) and *E.coli* iAF260(189). The content of LPS (Lipopolysaccharides), inorganic ions, peptidoglycan (murein), and cofactors, prosthetic groups and others were assumed to be similar to the ones reported in *E.coli* iAF260 (189) . The following external metabolites were allowed to freely enter and leave the network for simulations of anaerobic growth on DSMZ 193 media: PO<sub>4</sub><sup>3-</sup>, CO<sub>2</sub>, Mn<sup>2+</sup>, Zn<sup>2+</sup>, Cu<sup>2+</sup>, Ca<sup>2+</sup>, Cl<sup>-</sup>, Co<sup>2+</sup>, K<sup>+</sup>, Fe<sup>2+</sup>, Fe<sup>3+</sup>, riboflavin, Mg, cytidine triphosphate, biotin, spermidine, thiamin, folate, vitamin B-12, pantothenate, pyridoxal phosphate, cobinamide, nicotinamide, and lipoate. Also acetate and sulfate were added as electron donor and acceptor, respectively.

#### **4.2.8 Total mRNA extraction**

Cells were harvested from the two sets of duplicate 900 mL chemostat run in parallel in two conditions as previously described (190). Briefly, cultures were centrifuged at 4°C for 15 min and pellets were flash frozen and stored at -80°C. The biomass thus obtained were mixed with *RNAlater* (Ambion) as previously described (191) and RNA was extracted with TRIzol (Sigma) as previously described (36).

Total RNA was purified with the MinElute PCR purification kit (Qiagen) prior to rDNase I (Ambion) digestion following the manufacturers' protocol, followed by an additional treatment with the MinElute PCR purification kit. The absence of genomic DNA contamination was verified by 16S rRNA gene analysis as described previously (191). Then the mRNA was isolated with the *MICROBExpress* kit (Ambion), following the manufacturer's protocol. Aliquots of the triplicate mRNA extracts were analyzed with Experion RNA HiSens kit (Bio Rad) for the efficiency of rRNA removal.

#### **4.2.9 Illumina sequencing and assembly of Illumina reads**

The mRNA extracts were used to prepare directional multiplex libraries using ScriptSeq™ v2 RNA-Seq library preparation kit (Epicentre) following the manufacturer's protocol and single end sequencing was done using Hi-Seq 2000. All the raw data generated by Illumina sequencing was quality checked by visualization of base quality scores and nucleotide distributions. Then the sequences were sorted out by trimming of reads and read filtering based on base quality score and sequence properties such as primer contaminations, N content and GC bias using PRINSEQ (192).

#### **4.2.10 Mapping mRNA reads**

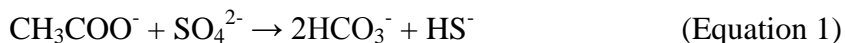
The mRNA sequence reads were first filtered for rRNA sequences and the purified mRNA reads were mapped against already published genome of *Desulfobacter postgatei* (DSM 2034) as described previously (35). For the final expression analysis, the mapped reads were normalized with the RPKM (reads assigned per kilobase of target per million mapped reads) method (193, 194) using ARRAY STAR. Reads from biological

replicates were first compared with each other graphically after mapping onto the template genomes. Biological replicates were highly reproducible (Figures C42a and C42b). Therefore, reads from biological replicates were merged and averaged for all further analysis. Expression levels were considered significant only when the  $\log_2$  RPKM value was  $\geq$  median RPKM value (Figure C42c; Table C18). In the co-culture fold changes were computed only for those genes that had  $\geq$  median RPKM in one of the samples.

## 4.3 Results and discussion

### 4.3.1 Energy metabolism

Biochemical analyses have shown *D. postgatei* couples the oxidation of acetate to the reduction of sulfate through a citric acid cycle, running in reverse (141) (see Appendix C, Figure C1). The stoichiometry of this reaction has a free energy change of -63 kJ per mol of acetate (Equation 1) (141). Since ADP phosphorylation in living cells costs around 70 kJ per mol of substrate (195, 196), previous calculations based on information available before the genome of *D. postgatei* was sequenced predicted that the metabolism should yield a net production of 0.9 mol of ATP per mol of acetate oxidized (197, 198). However, it was difficult to envisage such net production of ATP due to the fact that only 1 ATP per mol of acetate is produced via substrate phosphorylation (153) and there is a requirement of 2 ATP in the activation of sulfate to APS (199).



The question arises of how the electron flow is coupled to the generation of ATP in the metabolism of *D. postgatei*. In order to explain this, Rabus and colleagues (2006) suggested that proton translocation might take place during the reduction of NADP by ferredoxin and the following reduction of quinones by NADPH, allowing an extra production of ATP via chemiosmosis (Figure C7). This hypothesis was based on previous

biochemical experiments that suggested that *D. postgatei* has both succinate dehydrogenase, an enzyme that oxidizes succinate to fumarate, and a membrane-bound NADPH:menaquinone oxidoreductase, an enzyme that reoxidize the NADPH<sup>+</sup> generated during isocitrate oxidation (152, 198) (Figure C7). Although a ferredoxin:NADP oxidoreductase activity was mainly recovered in the membrane associated fraction, this enzyme was shown not to be involved in proton translocation (198).

Surprisingly, we could not find any homolog for genes encoding NADPH:menaquinone oxidoreductase and ferredoxin:NADP oxidoreductase in the genome sequence of *D. postgatei*. Instead, we found homologs encoding the complete set of subunits of three novel complexes that are related to energy conservation in other species and were not previously described in SRB. The novel complexes are the following: Quinone reductase (Qrc complex), Ech-hydrogenase-related complex (Ehr complex), and H<sup>+</sup>-translocating ferredoxin:NAD<sup>+</sup> oxidoreductase (Rnf complex). We also found 2 additional complexes that have been previously described in SRB, the Quinone-interacting oxidoreductase (Qmo complex), and the Ferredoxin:NADP oxidoreductase (Nfn complex). All of these complexes have subunits that are predicted to be membrane-bound by TMHMM Server v. 2.0 (<http://www.cbs.dtu.dk/services/TMHMM-2.0/>), with the exception of Nfn complex.

### **4.3.2 Novel membrane-bound complexes found in the genome of *D. postgatei***

#### **4.3.2.1 Qrc (Quinone-reductase) complex**

The membrane-associated Quinone Reductase Complex (Qrc) is composed of four subunits, three periplasmic (QrcABC) and one integral membrane subunit (QrcD). QrcA and QrcB are both membrane-anchored proteins (166). QrcA contains five or six heme binding motifs that interact with *c*-type cytochromes (166). QrcB belongs to the molybdopterin oxidoreductase family, and QrcC contains sixteen conserved Cys residues that binds four Fe-S clusters (161). These clusters are essential for electron transfer between the quinone pool and the catalytic center of the protein. QrcD is an integral membrane protein that belongs to the NrfD/PsrC family (166).



Qrc complex is widely found in other sulfate-reducing *Deltaproteobacteria*, such as *Desulfovibrio vulgaris* and *Desulfobacterium autotrophicum*, however its characterization has been limited to *D. vulgaris* (161). In *D. vulgaris*, periplasmic hydrogenases oxidize hydrogen and donate electrons to periplasmic  $c_3$  cytochromes. Then, *D. vulgaris* Qrc complex transfers electrons from the reduced pool of  $c_3$  cytochromes into the quinone pool (161).

The four subunits of the Qrc were found in the genome of *D. postgatei*. As in *D. vulgaris*, the genes encoding the four sub-units of this complex, *qrcA*, *qrcB*, *qrcC* and *qrcD* are located contiguously on the *D. postgatei* chromosome (Figure 12). Also, the membrane anchored QrcB belongs to the MopB superfamily of proteins, and QrcC has four Fe-S binding motifs. Moreover, the transmembrane-spanning QrcD corresponds to a polysulphide reductase that is predicted to be directly involved in the electrogenic interaction with the quinone pool (161). QrcA corresponds to a cytochrome that in *D. postgatei* and other SRBs contain five heme binding sites, and *D. vulgaris* has six. Surprisingly, the main difference between these complexes is that while the catalytic center (hemes) of the QrcA of *D. vulgaris* is located in the periplasm, in *D. postgatei* is predicted to be located in the cytoplasm (Figure 12). This particular localization of the hemes led us to envisage that the function of the Qrc complex in *D. postgatei* is to oxidize quinones and to reduce the cytoplasmic thiol/disulfide containing protein, DsrC, which is known to interact closely with the cytosolic enzyme dissimilatory sulfite reductase, DsrAB (157). This resembles the function of the Alternative complex (ACIII) described for *Rhodothermus marinus* (200) and *Chloroflexus aurantiacus* (201), a six to eight subunits membrane-bound complex, with the exception that in the Qrc complex the heme-binding sites are located in the cytoplasm. The difference in the localization of QrcA remains similar when comparing the sequences of other  $H_2$ -oxidizing and acetate-oxidizing SRBs suggesting that this modification may be widespread in other  $\delta$ -Proteobacteria (Figure 12). Therefore, we hypothesize that *D. postgatei* Qrc complex reduces the soluble DsrC with electrons coming from the quinone pool, coupling the opposite reaction than the one characterized in *D. vulgaris* (Figure 13).

#### 4.3.2.2 Ehr (Ech-hydrogenase-related) complex

The ability to oxidize hydrogen is a common feature in the metabolism of several SRBs (143, 202). For instance, H<sub>2</sub>-oxidizing SRB, such as *D. vulgaris* and *D. desulfuricans* possess both periplasmic and cytoplasmic hydrogenases (202). Besides its utilization as electron donor, hydrogen has been hypothesized to be involved in a mechanism called “chemiosmotic H<sub>2</sub> cycling” proposed by Odom and Peck (203). During this process, the reducing power resulting from the oxidation of organic acids is transferred to a membrane-bound hydrogenase (Ech) to generate H<sub>2</sub>. This gas diffuses to the periplasm and its re-oxidation produces electrons that are shuttled back to the cytoplasm by the Qrc complex. The main goal of this process is to contribute to energy conservation via H<sup>+</sup> translocation (203, 204) (Figure 14).

Ech hydrogenases belong to the subgroup of multisubunit membrane-bound energy-conserving [NiFe] hydrogenases and has been found in many SRB, such as *D. vulgaris* (205), *D. gigas* (204), and *Desulfotomaculum ruminis* (206) and also methanogens, such as *Methanosarcina barkeri* (207). Surprisingly, we did not detect Ech hydrogenases in the genome of *D. postgatei*. Instead, an Ech-hydrogenase-related (*ehr*) cluster (DespoDRAFT\_01512 - DespoDRAFT\_01517), previously described in *G. sulfurreducens* (208), was identified. Although sharing similar subunits with high homology, Ech-hydrogenase-related complex is not a [NiFe] hydrogenase because they lack the CxxC motifs containing the cysteine residues key for H<sub>2</sub> oxidation at the N and C terminus of EhrL, the large subunit of the complex (Figures C3 and C4) (208, 209). Although the subunit *D. postgatei* EhrS subunit is 52% similar to the one in *G. sulfurreducens*, its physiological function remains to be revealed. The N-terminal of these subunits seems to be related to Fe-S clusters suggesting that ferredoxins generated during acetate oxidation can be reoxidized with transfer of electrons into the quinone pool in the membrane. Since this is a membrane-bound complex and interacts with Qrc complex, this reaction is a likely to contribute to energy conservation (Figure 15).

To test whether H<sub>2</sub> cycling is important for energy conservation in *D. postgatei*, 10 ppm of hydrogen was supplied to the headspace of growing cultures. There was no hydrogen consumption after the culture was in stationary phase (120 hours), ruling out

the ability of periplasmic hydrogenases to oxidize hydrogen (Figure C8). This result agreed with recent evidence that showed that this process is not important for energy conservation in the closely related *Desulfovibrio alaskensis* (210). Although, this supports our hypothesis that “chemiosmotic H<sub>2</sub> cycling” is not important in *D. postgatei*, further experiments are required to establish the role of this enzyme in energy conservation.

#### 4.3.2.3 H<sup>+</sup>-translocating ferredoxin:NADP<sup>+</sup> oxidoreductase (Rnf complex)

It was suggested previously that SRB may be able to use electron bifurcation and confurcation to equilibrate reducing equivalents derived from the central metabolism (163, 211). In recent years, the Rnf complex (for *Rhodobacter* nitrogen fixation) has been identified in several microorganisms, including many SRB, suggesting it might be involved in energy conservation. The function of this complex is to provide a link between ferredoxin and NAD(H)/NADP(H) pools (161, 163, 212-217).

Genes encoding the six subunits of the proton-translocating ferredoxin:NADP<sup>+</sup> oxidoreductase (rnfABCDE) were found in one operon in the genome of *D. postgatei* (Figure C5). As reported for the methanogen *Methanosarcina acetivorans*, a multiheme cytochrome *c* encoding gene with 4–10 hemes was found next to the *rnf* genes (207). Also this *c*-type cytochrome is 71% identical of HRM2\_32060 and 28% identical to Dole\_2831, a *c*-type cytochrome found after one of the two copies of the *rnf* genes found in the close relatives *Desulfobacterium autotrophicum* and *Desulfococcus oleovorans* Hxd3, respectively (163). In agreement with previous research that showed that *D. postgatei* has a membrane-bound ferredoxin:NADP oxidoreductase, we predict that the Rnf complex of *D. postgatei* is involved in the reoxidation of ferredoxin, generated during 2-oxoglutarate oxidation, to the reduction of NAD<sup>+</sup> (198). Although previous studies suggested this enzyme was electrically independent, we hypothesized that *D. postgatei* Rnf is involved in proton-motive force generation by the translocation of either protons or sodium ions (Figure 16) (161).

A detailed description of other aspects of the metabolism of *D. postgatei* is provided in Supplementary data (Appendix C).

### 4.3.3 In silico metabolic model of *D. postgatei*

The manually curated genome was utilized to prepare a genome scale network of the metabolism of *D. postgatei*. The main reconstruction procedure was made following the published protocol [32]. The initial automatic reconstruction made by the rapid annotation using subsystem technology (RAST) server [33] and Model SEED pipeline [34] was further refined by using published biochemical and physiological information. After the model was improved through several iterations of hypothesis generation, the current version contains a matrix with 1084 reactions and 1025 metabolites, including 630 gene-protein-reaction associations.

The metabolic capabilities of the *D. postgatei* network were calculated using flux balance analysis and linear optimization. Energy conservation was calculated as shown in Table C2 (Appendix C). Biomass synthesis was selected as the objective function to be maximized in growth simulations. The biomass function describes the rate at which all of the biomass precursors are made in the correct proportions and also includes growth-associated energy demand (218). This reaction was constructed based on measurements of *D. postgatei* biomass composition (Appendix C, tables C3 to C14) and takes into account the amounts of 79 metabolites, cofactors, precursors, and ions required to synthesize each gram (dry weight) (gdw) of biomass, the proton consumed for reductive reactions, the ATP required for the polymerization (peptide biosynthesis, DNA replication, and RNA polymerization) and biosynthesis of precursors and metabolites. Energy parameters of the metabolic model including GAM (Growth-Associated Maintenance energy) (Tables C13 and C14), and NGAM (Non-Growth Associated Maintenance energy) were also determined (219). The GAM requirement for the *D. postgatei* model was calculated using empirical and physiological information and was equal to 59.72 mmol ATP/gdw h. The NGAM requirement (0.38 mmol ATP/gdw h) was estimated by fitting  $Y_{\text{ATP}}$  to the hypothetical zero growth condition as described by Pirt (1965) and others (219-221) (Figure C21).

The electron donors (acetate) or acceptors (sulfate) tested were allowed a maximum uptake rate into the network of ~5 mmol/gdw h or as specified in the results. All the simulations resulted in flux values in units of mmol/gdw h.

#### **4.3.4 Growth kinetics and stoichiometry under electron donor and electron acceptor limitation**

In order to better understand the dynamic of growth of *D. postgatei*, chemostats were run under nutrient limiting conditions and dilution rates between 0.014 and 0.032 h<sup>-1</sup>. Under electron donor limitation, basal medium was supplemented with 21.1 mM of sulfate as electron acceptor and 8.5 mM of acetate as electron donor.

The steady state concentrations of acetate were below detection limit at the lower dilution rates indicating that growth was limited by acetate. Up to 7.9 mM of sulfide was produced as a result of sulfate reduction; however this concentration did not seem to affect growth. An average of 13.7 mM of sulfate remained in the medium, indicating the 1:1 stoichiometry of acetate oxidation and sulfate reduction (Equation 1) (Figure C10). Consistent with Monod-type growth, the total biomass remained constant in the range of 44 to 50 mg dw/l and the biomass productivity was linear ( $r^2=0.96$ ) (Figure C9). Growth yield was equal to 5.7 g dw per mmol of acetate consumed (Table C15), slightly higher than 4.3-4.8 g dw per mmol of acetate previously reported on batch cultures (152, 154, 197). Both the specific respiration rate ( $q_{\text{electron}}$ ) and specific acetate consumption rates ( $q_{\text{acetate}}$ ) increased linearly with growth rate in both conditions tested (Figure C11). The efficiency of both acetate and sulfate metabolisms were higher when cultures were limited by acetate, suggesting that electron donor limitation may be more likely to occur in many sedimentary environments where *D. postgatei* is found (154).

Under limitation of sulfate, basal medium was supplemented with 8.5 mM of sulfate as electron acceptor and 21.1 mM of acetate as electron donor. Up to 9.5 mM of sulfide was accumulated in the medium, and an average of 13.7 mM of acetate remained (Figure C10). Sulfate concentration remained at steady state levels only under the lower dilution rates and the total biomass remained constant ~20% lower than acetate-limiting

growth suggesting a more substantial impact on the metabolism of *D. postgatei*, (Figure C12). Biomass productivity remained linear in all dilution rates ( $r^2=0.95$ ).

To the best of our knowledge, *D. postgatei* is not able to assimilate carbon through CO<sub>2</sub> fixation as can its close relative, *Desulfobacter hydrogenophilus* (222). Overall there was ca. 11% assimilation of acetate, which is consistent with other SRB. Under electron donor-limited growth, the majority of acetate (7.4 mM) was funneled into dissimilatory pathways, whereas under electron acceptor-limited growth an smaller fraction (6.3 mM) was used for dissimilation (Tables C15 and C16). This suggests that electron acceptor limitation affected growth more negatively than electron donor limitation.

Growth yield ( $Y_{ATP}$ ) is a parameter that illustrates how energy can be diverted in several cellular functions other than cell growth. These functions include metabolic pathways shifting, energy spilling, cell motility, osmoregulation, and turnover of macromolecular compounds, among others (221, 223, 224). The  $Y_{ATP}$  (mmol ATP/g dw h) increased linearly with the growth rate in both electron donor and electron acceptor limited cultures (Figure C21). The  $Y_{ATP}$  values were slightly higher for electron acceptor limited cultures, suggesting that limitation of sulfate required an additional energy input.

Microscopic examination (TEM) revealed that dividing cells were more abundant in the samples collected from *D. postgatei* growing at 0.032 h<sup>-1</sup> (Figures C17 and C19). Also, we observed smaller-diameter flagellated cells at dilution rates of 0.014 h<sup>-1</sup> as it was observed in similar studies (Figures C18 and C20) (225).

#### **4.3.5 Kinetic of acetate oxidation and sulfate reduction**

The half saturation constant ( $K_s$ ) obtained by Lineweaver-Burk linearization for acetate was 42 μM (Figure C14). This is in agreement with values previously reported (154, 226) and confirms that *D. postgatei* is able to deplete acetate to concentrations that are lower than those produced by most acetoclastic methanogens where sulfate is depleted (143, 226-228). The *D. postgatei* genome contains a gene encoding an acetate permease (DespoDRAFT\_03458; AcpA) that transports acetate from the environment to the cytoplasm together with protons (229). The half saturation constant of sulfate (81

$\mu\text{M}$ ) (Figure C16) suggests that in marine environments, where *D. postgatei* was originally isolated, the supply of acetate is more limited than sulfate (154).

#### 4.3.6 Validation of the metabolic model with experimental data

Simulations with the *D. postgatei* metabolic model were utilized to make predictions of *D. postgatei* metabolism. An initial *in silico* characterization of a batch-type growth indicates that the model utilizes acetate as the electron donor and sulfate as the electron acceptor, producing hydrogen sulfide as the end product. Other compounds in the culture medium, such as ammonia, were minimally used (Figure C22). This confirms that the metabolic model is able to resemble energy conservation through coupling acetate oxidation to sulfate reduction.

The *D. postgatei* metabolic model was validated by comparing experimental results obtained with chemostats with predicted results from *in silico* simulations. Under electron donor limitation, the predicted values matched well with the experimental data (Figure C23). The average of both experimental and predicted growth yields ( $n=6$ ) for *D. postgatei* growing under acetate limitation was 0.173 mg dw per mM of acetate. However, during sulfate-limiting conditions the predicted growth yield is 0.2 mg dw per mM of sulfate, while the experimental growth yield is 0.32 mg dw per mM of sulfate (Figure C24). This suggests that the metabolism of *D. postgatei* contains other pathways capable of improving the growth yield under electron acceptor limitation that our simulations in the metabolic model do not represent.

The properties of the *D. postgatei* model were further analyzed by Phenotype Phase Planes analysis (PhPP). This analysis aims to study the genotype-phenotype relation, describing the effect of the availability of two key substrates, acetate and sulfate, on the specific growth rate (230, 231). Growth rates of all predicted phenotypes under electron donor limitation were higher than the ones under electron acceptor limitation (Figure 17). Acetate-limited and sulfate-limited growth predictions resulted in five and four different phases, respectively (Figure 17). Each of these phases corresponds to a distinct region that is representative to a metabolic state of the metabolic model. The bottom phases (number 1 in both charts) correspond to unfeasible phenotypes with

specific growth rates close to zero due to the fact that either acetate- and sulfate- specific respiration rates are not enough to meet both biosynthesis of metabolites and ATP maintenance requirement. Regions 2 and 3 correspond to phenotypes to regions limited by the excess of acetate and sulfate, respectively. Region 4 is the area where acetate and sulfate are perfectly balanced and specific growth rate is close to highest. The plateau observed in the acetate-limited simulations suggested that under high access to acetate and sulfate, the set of reactions included in the model can act as ATP-consuming futile cycles (i.e. anapleurotic reactions) (Figure C1). Thus, the *D. postgatei* metabolic model has been validated with physiological data and can be applied in future modeling studies.

#### **4.3.7 *In silico* characterization of *D. postgatei* metabolism**

Examination of the metabolic model revealed that the citric acid cycle was the main source of electrons and reducing equivalents that are directed toward sulfate reduction. Considered a “specialist” acetate-oxidizing bacteria, *D. postgatei* has a cascade of reactions involved in acetate activation capable of acting as anapleurotic pathway to ensure the feeding of central metabolism, and also serving as an alternative futile cycle.

In order to gain a better understanding of the metabolic role of these anapleurotic reactions, the flux distribution of reactions in acetate and sulfate-limited chemostats at different growth rates (0.014–0.032 h<sup>-1</sup>) were examined in detail (Figure C25). In all cases, acetate was predicted to almost exclusively be utilized by succinyl:acetate CoA transferase (~95%) that funnels acetate into citric acid cycle, and small flux was routed to anapleurotic reactions. Indeed, both acetate-CoA ligases (AMP- and ADP-forming) were predicted to be active only under the highest growth rates. Synthesis of pyruvate through acetate kinase, phosphotransacetylase, and pyruvate ferredoxin oxidoreductase were linearly correlated with growth rates in order to meet the increasing requirements of gluconeogenic demand. The flux of these reactions was higher under sulfate-limited conditions, suggesting that these could be utilized as a potential futile cycle and there was more acetate available to fuel biosynthesis pathways. The highest portion of this flux is funneled into oxaloacetate by pyruvate carboxylase towards the biosynthesis of aspartate, asparagine, methionine, threonine, isoleucine, and lysine (Figure C25).



The correlation between the flux of both the citric acid cycle and the sulfate reduction pathway with growth rates in both acetate and sulfate limited simulations (Figures C26 to C37, Number 1 and 2) indicates that both pathways are the source of electrons and reducing equivalents towards energy conservation. However during sulfate limitation the flux of both pathways for each growth rate tested was higher, suggesting that there was an increased energy requirement. This result is consistent with the chemostats studies that showed a lower biomass under electron acceptor limitation (Table C16).

*D. postgatei* can conserve energy through chemiosmosis and substrate-level phosphorylation by ATP synthase and ATP-citrate lyase, respectively (198). The *D. postgatei* metabolic model predicts that the ATP synthase and ATP-citrate lyase, have the highest flux (7.69 mmol /gdw h and 6.9 mmol /gdw h, respectively) in cells growing at 0.032 h<sup>-1</sup> under sulfate limitation (Figures C26 to C37, Number 1 and 4). The flux predicted for acetate-limited growth was 15% lower for ATP synthase and 31% lower for ATP-citrate lyase, confirming the capability of the model to reflect the higher efficiency of *D. postgatei* to incorporate carbon into biomass under electron donor limitation. Furthermore, the flux predicted for both reactions correlated well with the growth rates under both conditions (acetate and sulfate limitation) (Figures C26 to C37, Number 1 and 4).

Interestingly, similar correlation to growth rates were observed for the flux distribution predicted for majority of the novel membrane-bound complexes found in *D. postgatei*. For instance, the Ehr (Ech-hydrogenase-related) complex, the membrane-bound enzyme capable of coupling oxidation of ferredoxins to the reduction of quinones, has a highest predicted flux under sulfate limitation (4.32 mmol /gdw h), while under acetate-limited growth the predicted flux was 34% lower (Figures C26 to C37, Number 6). Both the Qrc (Quinone-reductase) complex and the menaquinol:DsrC oxidoreductase (DrsDSRMKJOP) complex, which their hypothesized function is to oxidize quinones and reduce the cytoplasmic electron carrier, DsrC (Figure 13), have the highest predicted flux of 2.53 mmol /gdw h under sulfate limitation growing at 0.032 h<sup>-1</sup>. This value is also higher (48%) than the one predicted under acetate-limiting growth (1.7 mmol /gdw h). In agreement with our hypothesis based on the genome analysis, the flux through reactions

that connects the oxidation of ferredoxins (Qrc and Ehr) and quinones (DsrMKJOP) to the reduction of sulfate correlated well with growth rates under both conditions suggesting that these enzymes might also be linked to energy conservation.

The *D.postgatei* model predicted that the flux of the soluble Nfn (NADH-dependent reduced ferredoxin:NADP<sup>+</sup> oxidoreductase) complex was higher as respiration rates increases, suggesting that this enzyme plays an active role between ferredoxin and NAD(H)/NADP(H) pools (Figures C26 to C37, Number 7). On the other hand, the model predicts there is no flux through H<sup>+</sup>-translocating ferredoxin:NADP<sup>+</sup> oxidoreductase (Rnf complex) under all conditions utilized to simulate growth. Although this might reflect the incapability of the model to reproduce the intracellular physiological conditions, more experimental evidence is required to evaluate its involvement in energy conservation.

#### **4.3.8 Monte Carlo sampling of *D.postgatei* model**

Monte Carlo sampling is an approach to provide insights into the robustness of the genome-scale metabolic network by assessing and quantifying the impact of uncertainty on its predictions. Monte Carlo method (210, 232, 233) was used to examine the ability of the predicted fluxes to maintain specific functions in the face of varying conditions in the *D.postgatei* metabolic model. The flux distributions for a set of reactions were calculated from 2,200 possible solutions and plotted as histograms (Figures C38 to C41). Different trends appear in the distribution analysis of these reactions. For instance, the average flux distribution of the ATP-producing reactions, ATP citrate lyase and ATP synthase, followed a similar trend that the 2-oxoglutarate ferredoxin oxidoreductase, a key enzyme in the citric acid cycle (Figures C38 to C41, Numbers 1, 2 and 3). Also, the flux distribution of the Qrc (Quinone-reductase) complex and the Ehr (Ech-hydrogenase-related) complex followed a similar trend to the one for dissimilatory sulfite reductase (DsrAB) that catalyze the six-electron reduction of sulfite to sulfide (Figures C38 to C41, Numbers 4, 5 and 6). These results supported our previous hypothesis that the flux among all these reactions is likely to be linearly related, representing a high-flux-backbone involved in energy metabolism pathway of *D.postgatei*.

#### 4.3.9 Genome-wide transcriptional response of *D.postgatei* to different growth rates

In order to gain further insight into the physiological status of cells growing under electron donor limitation and to validate the computational predictions of *D. postgatei* metabolic model, the gene transcript abundance of *D. postgatei* growing in continuous culture at dilution rates of 0.032 h<sup>-1</sup> and 0.014 h<sup>-1</sup> was compared.

In general, transcript levels for genes encoding proteins involved in the central metabolism, sulfate respiration, amino-acid and protein biosynthesis were significantly higher as respiration rates increased. For instance, the gene encoding aconitase A (DespoDRAFT\_00181), the enzyme that catalyses the isomerization of citrate to isocitrate, was up-regulated as growth rates increased (Table 3). Also the genes encoding the alpha (DespoDRAFT\_00205), beta (DespoDRAFT\_00204), gamma (DespoDRAFT\_00203), and delta (DespoDRAFT\_00106) subunits of the 2-oxoglutarate:ferredoxin oxidoreductase (*kgor*) were also up-regulated (Table 3). This enzyme is often utilized in other anaerobes for the carboxylation of succinyl-CoA to 2-oxoglutarate (234). However in *D. postgatei* this enzyme couples the reverse reaction to the reduction of ferredoxins that are further utilized as reducing equivalents by the membrane-bound complexes Rnf and DsrMKJOP. Therefore, a ferredoxin encoded by DespoDRAFT\_00206 within the same operon is also up-regulated at the higher growth rate (Table 3). More interestingly, the gene encoding a succinyl-CoA:acetate CoA transferase, the enzyme that funnels the larger portion of acetate into the citrate acid cycle was also expressed in higher abundance at higher respiration rates (Table 3). The higher expression level of genes involved in the citric acid cycle under higher rate of metabolism agreed with the prediction made by the metabolic model.

Many genes encoding proteins associated with the sulfate reduction pathway were in higher abundance in cells growing at higher growth rates. For instance, the level of *dsrA* (dissimilatory sulfite reductase subunit  $\alpha$ ) transcripts, which has been proposed as proxy for the metabolic state of SRB (229, 235), was higher at the higher dilution rate (Table 3). The genes encoding four of the five subunits of the transmembrane DsrMKJOP complex (*dsrP*, *dsrO*, *dsrJ*, and *dsrK*) were also up-regulated (Table 3). This novel

complex is conserved in other SRB and has been predicted to link the quinone pool to the soluble DsrC cytochrome (See Appendix C), a key step in the reduction of sulfite. In contrast, lower transcript abundance for genes involved in the uptake of sulfate, such as sulfate permease-like transporter (DespoDRAFT\_02318), was found at the highest dilution rate, as compared with the lower dilution rate where ATP hydrolysis coupled to active transport is likely to be minimized (Table 3).

Since cultures at higher dilution rates have increased growth-associated energy consumption, higher levels of transcripts of genes involved in energy conservation were expected. Indeed, genes encoding five subunits of the ATP synthase (DespoDRAFT\_01538-01541 and DespoDRAFT\_01543) and three subunits of the proton-translocating ferredoxin:NADP<sup>+</sup> oxidoreductase (Rnf complex) were up-regulated at higher dilution rates (Table 3). This is in agreement with a proteogenomic study of sediments during *in situ* uranium bioremediation at a field study site in Rifle, CO, that found that proteins belonging to the *D. postgatei* Rnf complex were abundantly expressed in sediments after acetate stimulation (81). This supports our hypothesis that Rnf complex might be involved in coupling the reduction of ferredoxins to the translocation of protons. Furthermore, genes encoding four subunits of the quinone-reductase complex (Qrc) and the small subunit of the energy-converting hydrogenase related complex (*ehrS*) were also up-regulated supporting the model prediction that higher metabolic rates demand a higher flux through these reactions (Table 3).

It also appeared that protein biosynthesis was more important at higher growth rates, which was reflected in the higher abundance of transcripts encoding 50S (L2, L10, L14, L18, L20 and L35), 30S (S1, S6, S8, S11, S13, S16 and S21) ribosomal proteins, proteins involved in the aminoacylation of transfer RNAs (*aspS*, *leuS*, *gatA*), and proteins involved in amino acid biosynthesis (DespoDRAFT\_00630, DespoDRAFT\_00112, DespoDRAFT\_00823, DespoDRAFT\_01427, DespoDRAFT\_01742, DespoDRAFT\_01743, DespoDRAFT\_02637 and DespoDRAFT\_03545) (Table 3).

#### 4.4 Implications

Despite the central role that SRB plays in sulfur and carbon cycles and the number of sequenced genomes of SRB has increased significantly in the recent years, a deeper understanding of the energy metabolism and the electron transfer pathways of sulfate-reducing metabolism remained elusive. Recent studies have shown a range of novel components of the electron transfer pathways underlying the metabolism of SRB that include both novel membrane-bound and cytoplasmic enzymes (156, 157, 163, 165, 236, 237). However, all the experimental evidence has been limited to incomplete-oxidizing *Desulfovibrio* strains for which genetic tools are available.

This study presents three independent lines of evidence (genomic context, genome-scale metabolic network model and global transcriptional analysis) that identify novel enzymes involved in energy conservation. These included the energy-converting hydrogenase related complex, Ehr, the proton-translocating ferredoxin:NADP<sup>+</sup> oxidoreductase, Rnf, and also the NADH-dependent reduced ferredoxin:NADP<sup>+</sup> oxidoreductase, Nfn, that were not identified by previous biochemical studies (198). This new understanding of *D. postgatei* energy conservation will substantially improve the modeling of the growth of this organism in marine sediments and subsurface environments, and also shed light on the adaptation strategies that enable specialist microbes, such as *D. postgatei*, to succeed in such competitive niches (238).

Figures:

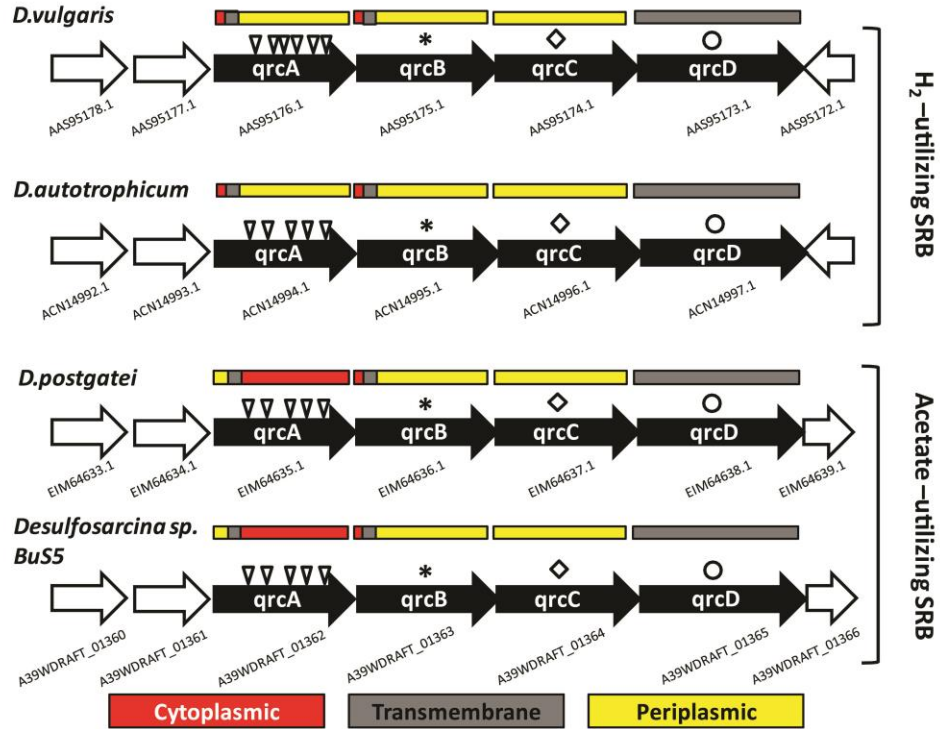


Figure 12: Comparison of the *D. postgatei* *qrc* operon to the one in *D. vulgaris*, *D. autotrophicum*, and *Desulfosarcina sp. BuS5*. Localization of the proteins was predicted by TMHMM Server v. 2.0 (<http://www.cbs.dtu.dk/services/TMHMM-2.0/>) (239). Regions predicted to be in the cytoplasm are shown in red. Regions predicted to be in the periplasm are shown in yellow. Transmembrane regions are shown in grey. Heme binding motifs are indicated by triangles. Proteins with Molybdopterin-Binding motifs are indicated by asterisks. Proteins containing domains which bind to iron-sulfur clusters are indicated by diamonds. Polysulphide reductases are indicated by circles.

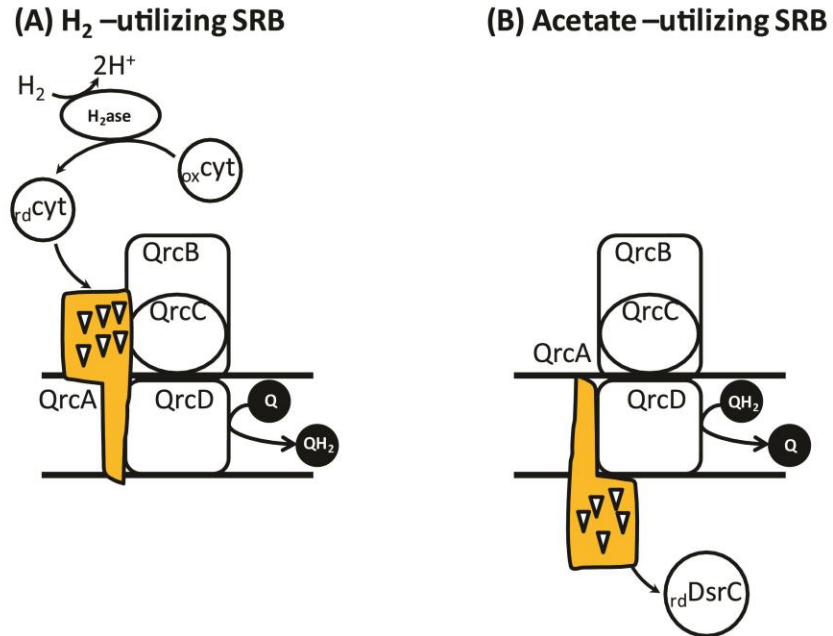


Figure 13: Representation of quinone reduction by Qrc in (A) H<sub>2</sub>-utilizing SRB (as *D. vulgaris*, see text) and the proposed cytochrome reduction by Qrc in (B) Acetate utilizing SRB. QH<sub>2</sub>, reduced quinone; Q, oxidized quinone; H<sub>2</sub>ase, periplasmic hydrogenase. Triangles indicate heme groups of the QrcA subunit.

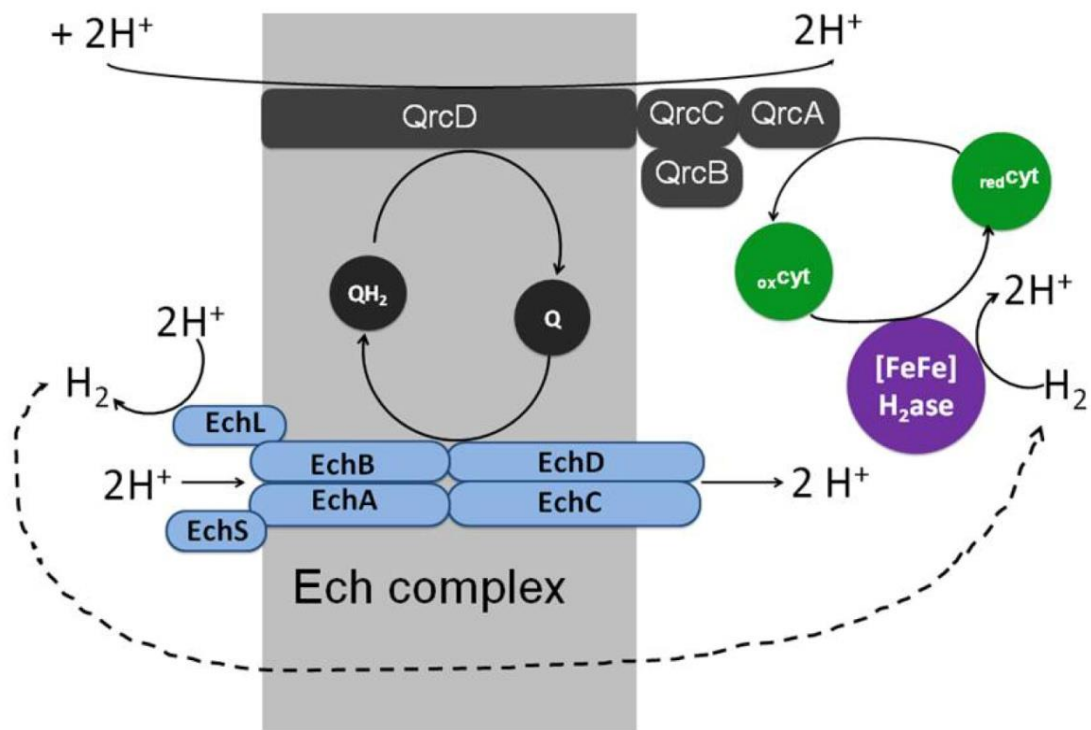


Figure 14: Hydrogen cycle in *D. vulgaris* proposed by Odom and Peck (203). Ech complex in blue and Qrc complex in gray. QH<sub>2</sub>, reduced quinone; Q, oxidized quinone; redCyt, reduced cytochrome, oxCyt, oxidized cytochrome; [FeFe] H<sub>2</sub>ase, periplasmic hydrogenase.



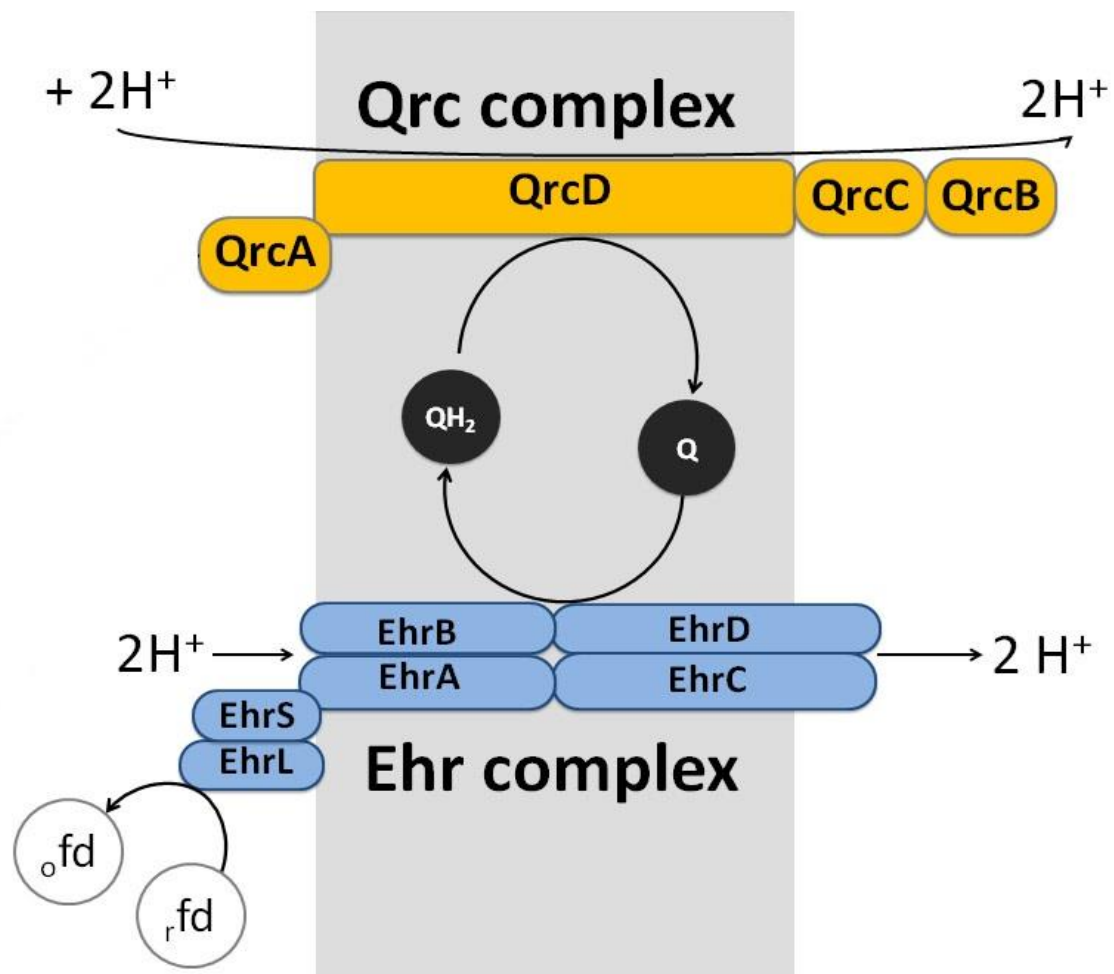


Figure 15: Predicted mechanism of Ehr complex and Qrc complex in *D. postgatei*. Ehr complex in blue and Qrc complex in gray.  $\text{QH}_2$ , reduced quinone;  $\text{Q}$ , oxidized quinone;

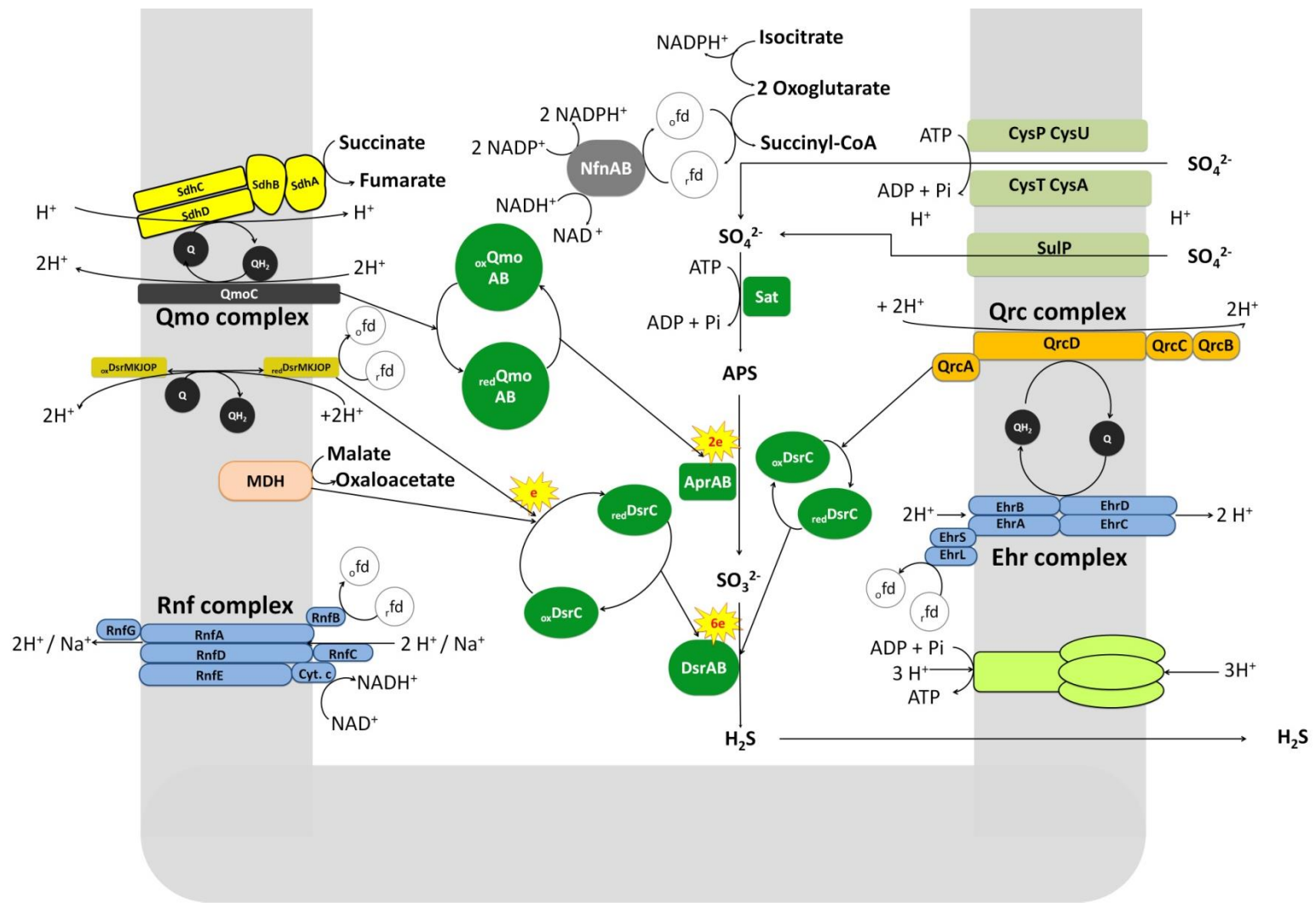


Figure 16: Schematic metabolic reconstruction of the energy metabolism of *D. postgatei*.

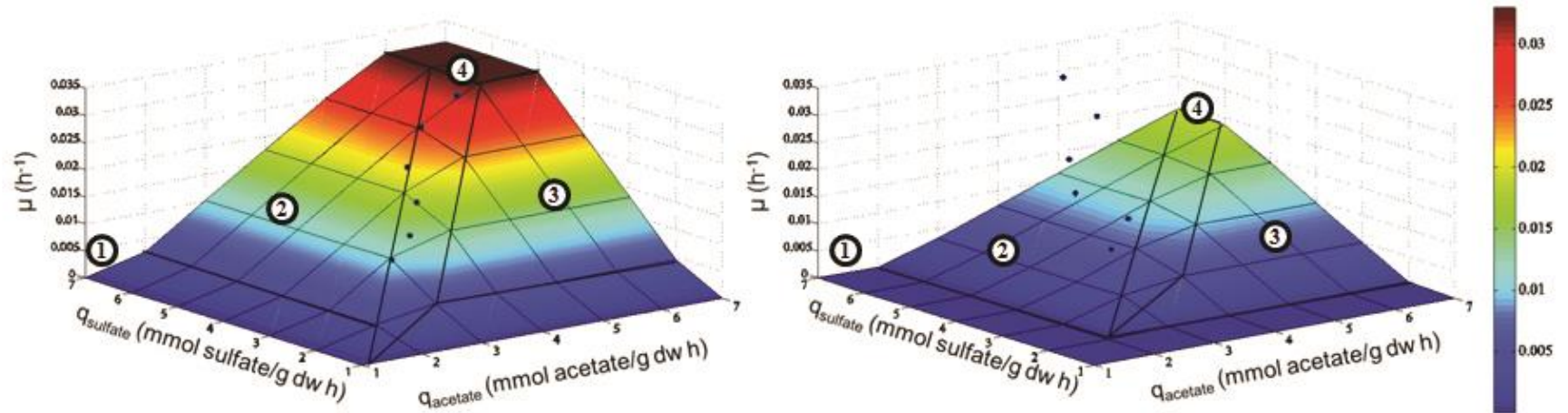


Figure 17: Phenotype Phase Planes analysis (PhPP) of *D. postgatei* metabolic model. The left graph corresponds to simulations made in acetate –limited growth and the right graph corresponds to simulations made in sulfate-limited growth. x-axis corresponds to sulfate specific respiration rate ( $q_{\text{sulfate}}$ ), y-axis corresponds to acetate specific respiration rate ( $q_{\text{acetate}}$ ), and z-axis corresponds to growth rate. Numbers indicate the different phases during growth

Table 3: Selected genes that were differentially expressed at least two fold in *D. postgatei* growing at 0.032 h<sup>-1</sup> compared to those growing at 0.014 h<sup>-1</sup> (P-value cutoff less than or equal to 0.05). Positive and negative numbers indicate up- and down-regulated genes at 0.032 h<sup>-1</sup>.

| Locus ID   | Gene Annotation  | Expression level (log2RPKM values) | P-value |
|--|--|------------------------------------|---------|
| <i>Central metabolism</i>                        |  |                                    |         |
| DespoDRAFT_00181                                 | aconitase A  | 2.55                               | 0.0261  |
| DespoDRAFT_00205                                 | 2-oxoglutarate:ferredoxin oxidoreductase, $\alpha$ subunit (kgorA) | 3.648                              | 0.0274  |
| DespoDRAFT_00204                                 | 2-oxoglutarate:ferredoxin oxidoreductase, $\beta$ subunit (kgorB)  | 3.356                              | 0.0463  |
| DespoDRAFT_00203                                 | 2-oxoglutarate:ferredoxin oxidoreductase, $\gamma$ subunit (kgorC) | 3.301                              | 0.0149  |
| DespoDRAFT_00106                                 | 2-oxoglutarate:ferredoxin oxidoreductase, delta subunit (kgorD)    | 2.619                              | 0.0138  |
| DespoDRAFT_00206                                 | ferredoxin   | 3.876                              | 0.0458  |
| DespoDRAFT_02073                                 | succinyl-CoA:acetate CoA transferase                               | 2.926                              | 0.0241  |
| <i>Sulfate reduction and energy conservation</i> |  |                                    |         |
| DespoDRAFT_01364                                 | sulfite reductase, dissimilatory-type alpha subunit (dsrA)         | 2.575                              | 0.0326  |
| DespoDRAFT_03015                                 | polysulfide reductase (dsrP)                                       | 5.123                              | 0.0175  |
| DespoDRAFT_03016                                 | Fe-S-cluster-containing hydrogenase                                | 4.233                              | 0.0455  |

|                  |   |        |         |
|------------------|---|--------|---------|
|                  | subunit (dsrO)  |        |         |
| DespoDRAFT_03017 | cytochrome c (dsrJ)   | 4.625  | 0.0447  |
| DespoDRAFT_03018 | Fe-S oxidoreductase (dsrK)  | 3.847  | 0.0218  |
| DespoDRAFT_02318 | Sulfate permease-like transporter (sulP3), high affinity sulfate transporter. | - 2.94 | 0.0209  |
| DespoDRAFT_01538 | ATP synthase F0 subunit b   | 2.432  | 0.00692 |
| DespoDRAFT_01539 | ATP synthase F1 delta subunit   | 2.823  | 0.0274  |
| DespoDRAFT_01540 | proton translocating ATP synthase F1 alpha subunit                            | 2.376  | 0.0449  |
| DespoDRAFT_01541 | ATP synthase F1 gamma subunit   | 2.627  | 0.0255  |
| DespoDRAFT_01543 | ATP synthase F1 epsilon subunit   | 2.708  | 0.0464  |
| DespoDRAFT_01996 | NADH:ubiquinone oxidoreductase $\delta$ subunit (rnfD)                        | 2.603  | 0.0247  |
| DespoDRAFT_01995 | electron transport complex RnfABCDGE type $\eta$ subunit (rnfG)               | 2.587  | 0.0014  |
| DespoDRAFT_01997 | NADH:ubiquinone oxidoreductase $\gamma$ subunit (rnfC)                        | 3.011  | 0.0361  |
| DespoDRAFT_02815 | class III cytochrome C family protein (qrcA)                                  | 2.754  | 0.0413  |
| DespoDRAFT_02816 | Anaerobic dehydrogenase typically selenocysteine-containing (qrcB)            | 2.341  | 0.0354  |
| DespoDRAFT_02817 | Fe-S-cluster-containing hydrogenase subunit (qrcC)                            | 3.301  | 0.0408  |
| DespoDRAFT_02818 | polysulfide reductase (qrcD)  | 3.166  | 0.0268  |

|                                |   |       |        |
|--------------------------------|---|-------|--------|
| DespoDRAFT_01512               | Ech-hydrogenase-related complex (ehrS)                  | 3.696 | 0.0355 |
| <i>Protein synthesis</i>       |   |       |        |
| DespoDRAFT_00756               | ribosomal protein L35                                   | 3.304 | 0.0161 |
| DespoDRAFT_00757               | ribosomal protein L20                                   | 2.163 | 0.0241 |
| DespoDRAFT_01792               | ribosomal protein S6                                    | 4.357 | 0.0338 |
| DespoDRAFT_02454               | ribosomal protein L10                                   | 2.625 | 0.0337 |
| DespoDRAFT_02465               | ribosomal protein L2<br>bacterial/organelar             | 2.002 | 0.0196 |
| DespoDRAFT_02472               | ribosomal protein L14<br>bacterial/organelle            | 2.351 | 0.0072 |
| DespoDRAFT_02476               | ribosomal protein S8                                    | 2.599 | 0.0431 |
| DespoDRAFT_02478               | ribosomal protein L18 bacterial type                    | 2.121 | 0.0498 |
| DespoDRAFT_02485               | 30S ribosomal protein S13                               | 2.231 | 0.0422 |
| DespoDRAFT_02486               | 30S ribosomal protein S11                               | 2.125 | 0.0466 |
| DespoDRAFT_02896               | ribosomal protein S16                                   | 2.795 | 0.0336 |
| DespoDRAFT_03026               | ribosomal protein S21                                   | 2.924 | 0.0355 |
| DespoDRAFT_03476               | ribosomal protein S1                                    | 2.468 | 0.0423 |
| DespoDRAFT_00157               | aspartyl-tRNA synthetase (aspS)                         | 2.694 | 0.0365 |
| DespoDRAFT_01802               | leucyl-tRNA synthetase (leuS)                           | 2.518 | 0.0315 |
| DespoDRAFT_02794               | glutamyl-tRNA(Gln) amidotransferase C<br>subunit (gatA) | 2.308 | 0.0418 |
| DespoDRAFT_02870               | glutamyl-tRNA synthetase                                | 5.392 | 0.0487 |
| <i>Amino acid biosynthesis</i> |   |       |        |

|                  |  |       |         |
|------------------|--|-------|---------|
| DespoDRAFT_00630 | 3-isopropylmalate dehydrogenase                              | 5.944 | 0.00598 |
| DespoDRAFT_00112 | branched-chain amino acid<br>aminotransferase, group II hisC | 5.158 | 0.0325  |
| DespoDRAFT_00823 | 3-isopropylmalate dehydratase, small<br>subunit              | 5.844 | 0.0439  |
| DespoDRAFT_01427 | aspartate/tyrosine/aromatic<br>aminotransferase              | 2.03  | 0.0248  |
| DespoDRAFT_01742 | phosphoserine aminotransferase                               | 6.266 | 0.0313  |
| DespoDRAFT_01743 | D-3-phosphoglycerate dehydrogenase                           | 4.408 | 0.0317  |
| DespoDRAFT_02637 | argininosuccinate synthase                                   | 2.676 | 0.0225  |
| DespoDRAFT_03545 | glutamate 5-kinase   | 2.354 | 0.0241  |

## CHAPTER 5

### CONCLUSION

This dissertation has presented three research projects with the goal of (1) investigating the electron transfer mechanism of *Geobacter sulfurreducens* to reduce U(VI), (2) evaluating the physiological response of *G. sulfurreducens* in the presence of environmental relevant concentrations of U(VI), and (3) understanding the physiology of energy conservation in the sulfate-reducing bacteria *Desulfobacter postgatei*. The integration of these goals seeks to improve our understanding about the interaction between *Geobacter* species, U(VI) and its competitor for acetate, *D. postgatei*, during *in situ* bioremediation of subsurface systems at a uranium-contaminated site in Rifle, CO.

The first research project described the nature of the molecular mechanism by which *G. sulfurreducens* reduces U(VI) through an integrative approach. Although, early studies with *G. sulfurreducens* suggested that outer-surface *c*-type cytochromes might play a role in U(VI) reduction (52), more recent evidence suggested that there is substantial U(VI) reduction at the surface of the electrically conductive pili known as microbial nanowires (60). We found that in order to reduce rates of U(VI) reduction to levels less than 20% of wild-type it was necessary to delete the genes for the five most abundant outer surface *c*-type cytochromes of *G. sulfurreducens*. Furthermore, a strain of *G. sulfurreducens*, known as Aro-5, which produces pili with substantially reduced conductivity, reduced U(VI) nearly as well as wild-type as did a strain in which the gene for PilA, the structural pilin protein, was deleted. We also observed through Transmission electron microscopy and X-ray Energy Dispersion Spectroscopy that wild-type cells did not precipitate uranium along pili as previously reported, but U(IV) was precipitated at the outer cell surface. Our findings are consistent with previous studies which have suggested that *G. sulfurreducens* requires outer-surface *c*-type cytochromes, but not pili, for the reduction of soluble extracellular electron acceptors.

The second research project described the physiological response of a mid-exponential phase culture of *G. sulfurreducens* exposed for four hours to 100  $\mu$ M of U(VI) by a global proteomic approach. This results were complemented with the



monitoring of several strains of *G.sulfurreducens* growing under the three following conditions: absence of U(VI), “slight U(VI) stress” (in the presence of 100  $\mu$ M of U(VI) in the form of uranyl acetate) and “severe U(VI) stress” (in the presence of 1mM of U(VI) in the form of uranyl acetate). We found that U(VI)-exposed cultures expressed lower levels of proteins involved in growth, protein and amino acid biosynthesis, as a result of the deleterious effect of U(VI). In contrast, proteins involved in detoxification, such as several efflux pumps belonging to the RND family, and protection of membrane and proteins, such as chaperons and proteins involved in secretion systems, were in higher abundance in cells exposed to U(VI). Exposing *G. sulfurreducens* to U(VI) resulted in higher abundance of many proteins associated with the oxidative stress response, such as superoxide dismutase and superoxide reductase. A strain in which the gene for superoxide dismutase was deleted grew slower than the wild-type strain in the presence U(VI), but not in its absence. The results suggest that there is not one specific U(VI)-detoxification system specific mechanism for uranium detoxification. Rather, resistance to U(VI) appears to be accomplished with multiple stress response systems and regulatory networks that facilitate fast adaptation to rapidly changing conditions. The ability of *Geobacter* species to cope with potential U(VI) toxicity in this manner may be one of the reasons that *Geobacter* species are often one of the most abundant genera of microorganisms during *in situ* uranium bioremediation.

The third research project described the physiology of the energy conservation in the sulfate-reducing bacteria *D. postgatei*, a pure culture model for the *Desulfobacter* species that play an important role in sulfate reduction in marine sediments and that have a negative impact on *in situ* uranium bioremediation by outcompeting U(VI)-reducing species for acetate. During this project the genome of *D. postgatei* was sequenced and a genome-scale metabolic model constructed. The annotated genome obtained from the Joint Genome Institute was manually curated, identifying 3773 genes predicted, 3678 of which were predicted to encode proteins. Growing *D. postgatei* in a continuous-culture system under electron donor (acetate) and electron acceptor (sulfate)-limiting conditions provided important physiological data and growth parameters that were incorporated into a genome-scale metabolic model designed to quantitatively explore energy conservation from acetate oxidation coupled to sulfate reduction. The model was improved through

several iterations of hypothesis generation, and integration of experimental and bibliographic data. Through this process, novel elements for energy conservation were discovered. These included the energy-converting hydrogenase related complex, Ehr, the proton-translocating ferredoxin:NADP<sup>+</sup> oxidoreductase, Rnf, and also the NADH-dependent reduced ferredoxin:NADP<sup>+</sup> oxidoreductase, Nfn. The current version of the model predicts that these complexes actively regulate the transition of the cells into different physiological states, providing also a link between the ferredoxin and NAD(H)/NADP(H) pools. RNA-seq analysis of transcript abundance in cells grown in an acetate-limited chemostat at different growth rates (0.014–0.032 h<sup>-1</sup>) revealed that many of the genes encoding proteins involved in these complexes were expressed in higher abundance as respiration rates increased. The future enzymatic characterization of these complexes as well as their interactions with recently characterized enzymes involved in energy conservation (156, 159, 163-165, 236, 237, 240), will increase our understanding of the energy metabolism and the electron transfer pathways of sulfate-reducing bacteria.

The many physiological aspects revealed in this dissertation expanded the physiological framework of *Geobacter* species, increasing the knowledge about microbe–radionuclide interactions and its potential as a powerful tool for *in situ* bioremediation. This dissertation increase the knowledge of the physiology of *D.postgatei* that can serve as a platform to improve our understanding of microbial interactions and their environments, allowing us to predict physiological status and behavior of these two species and tune the electron donor inputs along bioremediation of uranium-contaminated groundwater.

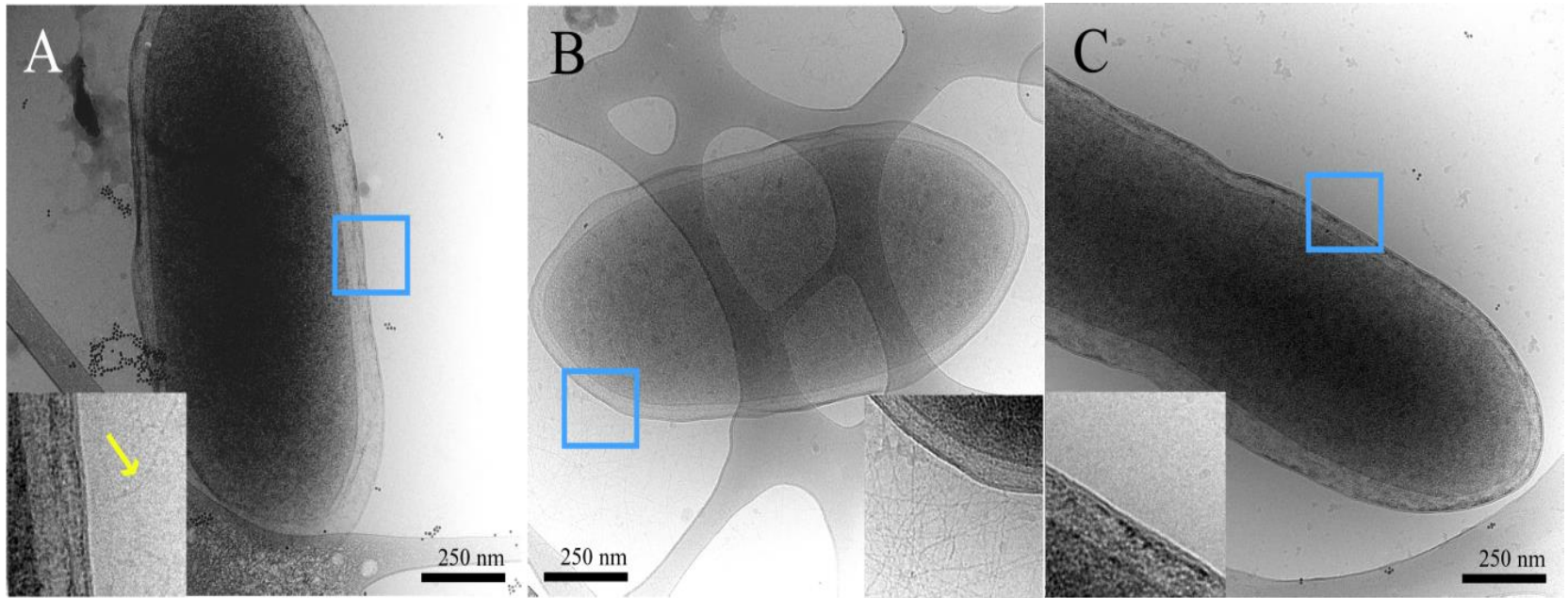
## **APPENDICES**

**APPENDIX A**

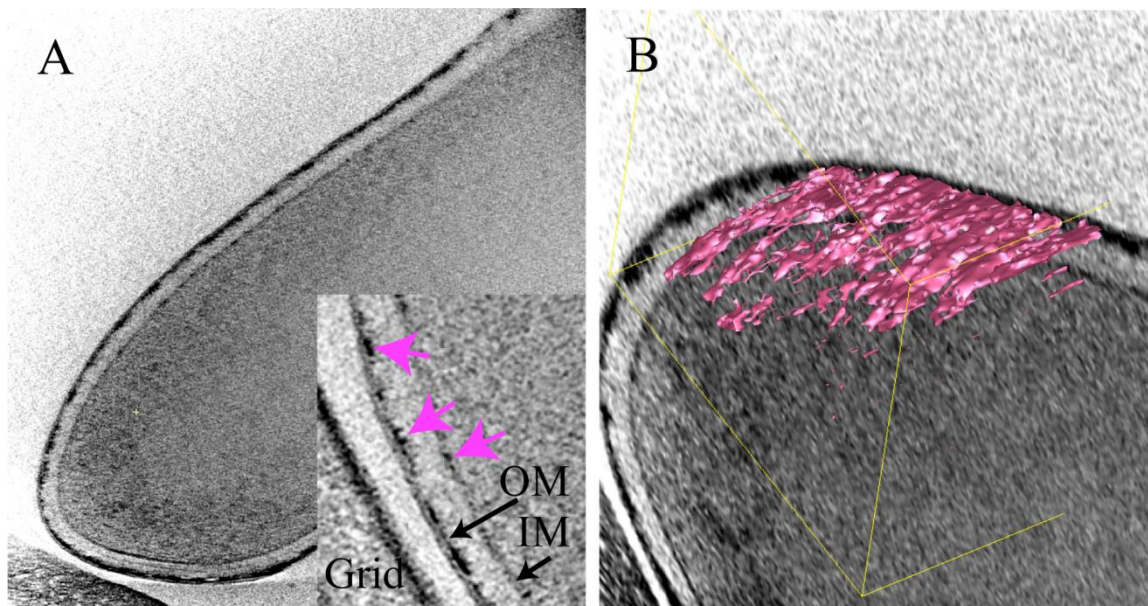
**SUPPLEMENTARY INFORMATION U(VI) REDUCTION BY A DIVERSITY OF  
OUTER SURFACE C-TYPE CYTOCHROME OF GEOBACTER  
SULFURREDUCENS**

Table A1: Strains used in this study.

| Strain name       | Deleted or modified gene(s)   | Genbank accession number of deleted or modified gene(s)         | Localization | Reference |
|-------------------|---|---|--------------|-----------|
| $\Delta$ omcST    | omcS; omcT is also not expressed  | GI-39997599   | OM           | (89)      |
| $\Delta$ omcZ     | omcZ  | GI-39997174   | OM           | (87)      |
| $\Delta$ pilA     | pilA  | GI-39996596   | OM           | (58)      |
| $\Delta$ pilA::cm | -   | -   | -            | (58)      |
| $\Delta$ BSTE     | omcB, omcS, omcT, omcE  | GI-39997831, GI-39997599, GI-39997598, GI-39995725              | OM           | (62)      |
| $\Delta$ BSTEZ    | omcB, omcS, omcT, omcE, omcZ  | GI-39997831, GI-39997599, GI-39997598, GI-39995725, GI-39997174 | OM           | (62)      |
| $\Delta$ aro-5    | Alanine was substituted for each of the five aromatic amino acids in the carboxyl terminus of pilA gene | GI-39996596   | C            | (88)      |



**Figure A1: CryoTEM images of (A) wild-type, (B)  $\Delta$ BESTZ, and (C)  $\Delta$ pilA cells respiring U(VI).** The cell walls and high contrast aggregates were discussed in the context of Fig. 6. We clearly see normal pili distribution in wild type, high abundance of pili in cells of  $\Delta$ BESTZ, and no pili in  $\Delta$ pilA. Insets show magnified views of small regions within blue boxes for enhanced view.



**Figure A2: Cryo-ET of  $\Delta pilA$  cells respiring U(VI).** **A)** Slice through a 3D cryo-ET reconstruction of an intact cell in vitreous ice. The high contrast encasing/spanning the OM is consistent with U deposition, the only high atomic number element (very “electron dense”) added to the cultures. IM: inner membrane; OM: outer membrane; Grid: carbon coated Formvar support. Pink arrows: aggregates at OM and IM. **B)** Slice through a 3D cryo-ET of another cell with. The isosurface rendering in 3D of a region of the high contrast aggregates is shown in dark pink, superimposed on a slice of the same cryo-ET reconstruction in grey-scale. The yellow box outlines the 3D isosurface sub-volume. See XEDS line scans across the cell surface and cell wall in **Figure 6B** unequivocally identifying the aggregates as U. Scale: the width of the periplasmic space is approximately 30 nm.

## APPENDIX B

### SUPPLEMENTARY INFORMATION PROTEOME OF GEOBACTER SULFURREducENS IN THE PRESENCE

Table B1: Proteins with increased abundance under U(VI) exposure.  $\Delta z$ -score was calculated as follows: (z-score in U treatment - z-score in control).

| Locus ID | Symbol | Name  | $\Delta z$ |
|----------|--------|---|------------|
| GSU2213  |        | GAF domain protein                                    | 1.82       |
| GSU2429  |        | peptidylprolyl cis-trans isomerase, PpiC-type         | 1.82       |
| GSU0014  |        | DnaJ-related molecular chaperone                      | 1.82       |
| GSU1737  | paaK-2 | phenylacetate-CoA ligase                              | 1.81       |
| GSU1482  |        | efflux pump, RND family, outer membrane protein       | 1.81       |
| GSU1458  |        | TPR domain protein                                    | 1.80       |
| GSU3318  |        | conserved hypothetical protein                        | 1.80       |
| GSU3246  | prx-2  | peroxiredoxin, typical 2-Cys subfamily                | 1.80       |
| GSU1183  |        | O-acetyl-L-homoserine sulfhydrylase                   | 1.80       |
| GSU1493  | pilC   | type IV pilus biogenesis protein PilC                 | 1.79       |
| GSU1919  | pyrH   | uridylate kinase                                      | 1.79       |
| GSU3292  |        | transcriptional regulator, Fur family                 | 1.79       |
| GSU0987  |        | conserved hypothetical protein                        | 1.79       |
| GSU1817  |        | outer membrane lipoprotein, Slp family                | 1.79       |
| GSU0106  |        | chromosome partitioning ATPase Soj                    | 1.79       |
| GSU3077  | mraW   | SAM-dependent membrane protein methyltransferase MraW | 1.78       |
| GSU3470  | dnaA   | chromosomal replication initiator protein DnaA        | 1.78       |
| GSU3424  |        | dihydrolipoamide dehydrogenase-related protein        | 1.78       |
| GSU2980  | nikR   | nickel-binding domain transcriptional regulator       | 1.78       |
| GSU0720  |        | superoxide reductase                                  | 1.78       |



|         |         |  |      |
|---------|---------|--|------|
| GSU0983 |         | phage-related baseplate assembly protein, putative                         | 1.78 |
| GSU2038 | pilY1-2 | type IV pilus tip-associated adhesin                                       | 1.78 |
| GSU1530 | hisG-1  | ATP phosphoribosyltransferase  | 1.77 |
| GSU2700 | tupA    | tungstate ABC transporter, periplasmic tungstate-binding protein, putative | 1.77 |
| GSU2666 |         | transcriptional regulator, TetR family                                     | 1.77 |
| GSU2695 |         | efflux pump, RND family, outer membrane protein                            | 1.77 |
| GSU0990 |         | hypothetical protein   | 1.77 |
| GSU1155 |         | glutaredoxin family protein  | 1.77 |
| GSU0672 |         | conserved hypothetical protein   | 1.77 |
| GSU0160 | dapB    | dihydrodipicolinate reductase  | 1.77 |
| GSU2516 |         | rhodanese homology domain pair protein                                     | 1.77 |
| GSU1328 |         | protein of unknown function DUF1255  | 1.76 |
| GSU0197 |         | oxidoreductase, short chain dehydrogenase/reductase family                 | 1.76 |
| GSU1090 |         | signal transduction protein-related protein, response receiver             | 1.76 |
| GSU2441 |         | conserved hypothetical protein   | 1.76 |
| GSU0457 |         | outer membrane lipoprotein LolB, putative                                  | 1.76 |
| GSU2821 | nifH    | nitrogenase iron protein   | 1.75 |
| GSU0689 | hpnN    | efflux pump, RND superfamily, putative                                     | 1.75 |
| GSU0357 |         | cytochrome c family protein  | 1.74 |
| GSU2425 |         | O-acetyl-L-homoserine sulfhydrylase  | 1.74 |
| GSU3066 | ddl     | D-alanine--D-alanine ligase  | 1.74 |
| GSU3296 | glcD-1  | D-lactate/glycolate dehydrogenase, FAD-binding protein, putative           | 1.74 |
| GSU0483 | queC    | 7-cyano-7-deazaguanine synthase  | 1.73 |
| GSU3373 | rsmB    | 16S rRNA (5-methyl-C967)-methyltransferase                                 | 1.73 |
| GSU2869 | secE    | preprotein translocase, SecE subunit                                       | 1.73 |
| GSU1648 | macC    | cytochrome c, 5 heme-binding sites   | 1.73 |
| GSU2062 |         | response receiver-modulated nucleotide cyclase                             | 1.72 |
| GSU1230 |         | ABC transporter, periplasmic substrate-binding protein                     | 1.72 |

|         |        |  |      |
|---------|--------|--|------|
| GSU2801 |        | cytochrome c, 5 heme-binding sites   | 1.72 |
| GSU1089 |        | iron-sulfur cluster-binding protein  | 1.72 |
| GSU1158 | sodA   | superoxide dismutase, iron/manganese-containing                                    | 1.72 |
| GSU1117 |        | response regulator   | 1.71 |
| GSU0800 |        | amino acid ABC transporter, periplasmic amino acid-binding protein                 | 1.71 |
| GSU2136 |        | efflux pump, RND family, membrane fusion protein                                   | 1.71 |
| GSU1459 | ispG   | 4-hydroxy-3-methylbut-2-en-1-yl diphosphate synthase                               | 1.71 |
| GSU0242 | acpP-1 | acyl carrier protein   | 1.71 |
| GSU1827 | nadB   | L-aspartate oxidase  | 1.71 |
| GSU0008 |        | response receiver sensor histidine kinase, PAS domain-containing                   | 1.71 |
| GSU3464 | gidA   | tRNA (5-carboxymethylaminomethyl-2-thio-U34)-formylglycyltransferase               | 1.71 |
| GSU2212 | cheY-5 | chemotaxis protein CheY  | 1.71 |
| GSU0783 |        | nickel-dependent hydrogenase, iron-sulfur cluster-binding protein                  | 1.71 |
| GSU2538 | nspC   | carboxynorspermidine decarboxylase   | 1.71 |
| GSU1729 |        | phenylacetate-CoA ligase   | 1.70 |
| GSU3072 | murF   | UDP-N-acetylmuramoylalanyl-D-glutamyl-2,6-diaminopimelate-D-alanyl-D-alanyl ligase | 1.70 |
| GSU1900 |        | transporter, putative  | 1.70 |
| GSU2265 | fabZ   | (3R)-hydroxymyristoyl-(acyl-carrier-protein) dehydratase                           | 1.70 |
| GSU0582 |        | methyl-accepting chemotaxis protein  | 1.70 |
| GSU1999 | hfq    | hfq protein  | 1.70 |
| GSU0869 |        | LysM domain/NLP/P60 family protein   | 1.69 |
| GSU1845 |        | conserved hypothetical protein   | 1.69 |
| GSU2437 |        | conserved hypothetical protein   | 1.69 |
| GSU2814 |        | rubrerythrin   | 1.69 |
| GSU2938 |        | conserved hypothetical protein   | 1.69 |

|         |        |  |      |
|---------|--------|--|------|
| GSU2477 |        | radical SAM domain-containing iron-sulfur cluster-binding oxidoreductase | 1.69 |
| GSU1606 | rpiB   | ribose-5-phosphate isomerase B, putative                                 | 1.68 |
| GSU3423 | tkt    | transketolase  | 1.68 |
| GSU3209 |        | protein of unknown function DUF143                                       | 1.68 |
| GSU2549 | topA   | DNA topoisomerase I  | 1.68 |
| GSU3117 | ssb-2  | single-strand binding protein  | 1.67 |
| GSU3134 |        | conserved hypothetical protein   | 1.67 |
| GSU1942 | capL   | UDP-N-acetyl-D-galactosamine 6-dehydrogenase, putative                   | 1.67 |
| GSU0601 |        | glycoside hydrolase, putative  | 1.67 |
| GSU1667 |        | conserved hypothetical protein   | 1.67 |
| GSU2569 | mnmA   | tRNA (5-carboxymethylaminomethyl-2-thio-U34)-thioltransferase            | 1.66 |
| GSU0865 |        | cell division protein DivIVA, putative                                   | 1.66 |
| GSU0505 |        | rhodanese homology domain superfamily protein                            | 1.66 |
| GSU1103 |        | AMP-forming acyl-CoA synthetase  | 1.66 |
| GSU0352 | prx-3  | peroxiredoxin, atypical 2-Cys subfamily                                  | 1.66 |
| GSU2923 | murI   | glutamate racemase   | 1.66 |
| GSU3278 |        | conserved hypothetical protein   | 1.66 |
| GSU1909 | ilvC   | ketol-acid reductoisomerase  | 1.66 |
| GSU1706 | panC   | pantoate--beta-alanine ligase  | 1.66 |
| GSU1548 |        | hypothetical protein   | 1.66 |
| GSU0290 | fabH-1 | 3-oxoacyl-(acyl-carrier-protein) synthase III                            | 1.65 |
| GSU1283 |        | conserved hypothetical protein   | 1.65 |
| GSU0867 | ubiE   | ubiquinone/menaquinone biosynthesis methyltransferase UbiE, putative     | 1.65 |
| GSU0157 |        | lipoprotein, putative  | 1.65 |
| GSU1778 | pulQ   | type II secretion system secretin lipoprotein PulQ                       | 1.65 |
| GSU1875 | ahcY   | S-adenosyl-L-homocysteine hydrolase                                      | 1.65 |
| GSU0478 |        | ferritin-like domain protein   | 1.65 |

|         |         |   |      |
|---------|---------|---|------|
| GSU3454 |         | radical SAM domain iron-sulfur cluster-binding oxidoreductase                     | 1.64 |
| GSU1584 | bioB    | biotin synthetase   | 1.64 |
| GSU0164 |         | conserved hypothetical protein, truncation  | 1.64 |
| GSU1679 |         | hypothetical protein  | 1.64 |
| GSU2781 |         | efflux transporter, RND family, MFP subunit                                       | 1.64 |
| GSU3410 |         | conserved hypothetical protein  | 1.64 |
| GSU2559 |         | exopolyphosphatase  | 1.64 |
| GSU1589 | rbfA    | ribosome-binding factor A   | 1.63 |
| GSU1836 | glnB    | nitrogen regulatory protein P-II  | 1.63 |
| GSU0585 | ycgM    | fumarylacetoacetate hydrolase family protein ycgM                                 | 1.63 |
| GSU3094 | hisE    | phosphoribosyl-ATP pyrophosphohydrolase   | 1.63 |
| GSU2101 |         | glycerol dehydratase, putative  | 1.63 |
| GSU0032 | grpE    | DnaJ adenine nucleotide exchange factor GrpE                                      | 1.63 |
| GSU2493 |         | NHL repeat domain protein   | 1.63 |
| GSU1270 | pyrR    | pyrimidine operon regulatory protein PyrR; uracil<br>phosphoribosyltransferase    | 1.63 |
| GSU0648 | rplS    | ribosomal protein L19   | 1.62 |
| GSU0345 | nuoH-1  | NADH dehydrogenase I, H subunit   | 1.62 |
| GSU2906 |         | conserved hypothetical protein  | 1.62 |
| GSU1614 |         | CoA-binding protein   | 1.62 |
| GSU2850 | rplP    | ribosomal protein L16   | 1.62 |
| GSU3010 | cobU    | adenosylcobinamide kinase and adenosylcobinamide phosphate<br>guanylyltransferase | 1.62 |
| GSU1066 | pilY1-1 | type IV pilus tip-associated adhesin  | 1.61 |
| GSU2008 |         | branched-chain amino acid ABC transporter, ATP-binding<br>protein                 | 1.61 |
| GSU2998 |         | conserved hypothetical protein  | 1.61 |
| GSU0604 | thiC-1  | 4-amino-5-hydroxymethyl-2-methylpyrimidine synthetase                             | 1.61 |
| GSU0152 | argF    | ornithine carbamoyltransferase  | 1.61 |
| GSU2761 |         | FAD-dependent glycerol-3-phosphate dehydrogenase subunit                          | 1.61 |

|         |        |   |      |
|---------|--------|---|------|
| GSU1415 |        | response regulator  | 1.61 |
| GSU0189 | dbpA   | ATP-dependent RNA helicase DbpA                                     | 1.61 |
| GSU2286 | eno    | enolase   | 1.60 |
| GSU2572 | cysE   | serine acetyltransferase  | 1.60 |
| GSU2718 | hoxL   | bidirectional NAD-reducing hydrogenase, large subunit               | 1.60 |
| GSU1708 |        | metal-dependent hydrolase, subgroup D                               | 1.60 |
| GSU1855 |        | polysaccharide chain length determinant domain protein              | 1.60 |
| GSU2051 | paaK-3 | phenylacetate-coenzyme A ligase                                     | 1.60 |
| GSU0933 | upp    | uracil phosphoribosyltransferase                                    | 1.60 |
| GSU0156 | argH   | argininosuccinate lyase   | 1.60 |
| GSU3109 |        | transcriptional regulator, IclR family                              | 1.60 |
| GSU1978 | epsI   | EpsI family protein   | 1.59 |
| GSU3457 |        | amino acid-binding ACT domain regulatory protein                    | 1.59 |
| GSU2013 |        | phosphoglucomutase/phosphomannomutase family protein                | 1.59 |
| GSU0599 |        | sensor histidine kinase   | 1.59 |
| GSU2383 | trpE   | anthranilate synthase component I                                   | 1.59 |
| GSU2106 |        | conserved hypothetical protein                                      | 1.59 |
| GSU2012 | nifU   | nitrogen fixation iron-sulfur cluster assembly protein NifU         | 1.59 |
| GSU0361 |        | peptidylprolyl cis-trans isomerase, PpiC-type                       | 1.59 |
| GSU1463 | aspS   | aspartyl-tRNA synthetase  | 1.58 |
| GSU2789 |        | sensor histidine kinase, PAS, PAS and PAS domain-containing         | 1.58 |
| GSU0384 |        | ferritin-like domain protein  | 1.58 |
| GSU1905 |        | cold shock domain family protein                                    | 1.58 |
| GSU1642 |        | ferritin-like domain protein  | 1.58 |
| GSU3395 | putA   | proline dehydrogenase/delta-1-pyrroline-5-carboxylate dehydrogenase | 1.58 |
| GSU3370 |        | transcriptional regulator, GntR family                              | 1.57 |
| GSU2431 | nfeD   | NfeD-like membrane-bound serine protease                            | 1.57 |
| GSU1632 | purB   | adenylosuccinate lyase  | 1.57 |
| GSU1626 |        | transcriptional regulator, GntR family                              | 1.57 |

|         |        |  |      |
|---------|--------|--|------|
| GSU3265 |        | sulfite reductase, assimilatory-type                           | 1.56 |
| GSU1427 |        | anti-anti-sigma factor   | 1.56 |
| GSU0496 |        | efflux transporter, RND family, MFP subunit                    | 1.56 |
| GSU0283 |        | sensor histidine kinase  | 1.56 |
| GSU0150 | argB   | acetylglutamate kinase   | 1.56 |
| GSU2045 | valS   | valyl-tRNA synthetase  | 1.56 |
| GSU2742 |        | conserved hypothetical protein                                 | 1.55 |
| GSU1467 | korD   | 2-oxoglutarate:ferredoxin oxidoreductase, ferredoxin subunit   | 1.55 |
| GSU0153 | argG   | argininosuccinate synthase                                     | 1.55 |
| GSU0099 | mglA   | cell polarity determinant GTPase MglA                          | 1.55 |
| GSU1432 |        | TPR domain protein   | 1.55 |
| GSU2029 | pilP   | type IV pilus assembly lipoprotein PilP, putative              | 1.55 |
| GSU2625 |        | transcriptional regulator, ArsR family                         | 1.55 |
| GSU1108 |        | aldehyde dehydrogenase family protein                          | 1.55 |
| GSU0312 |        | PilZ domain protein  | 1.55 |
| GSU0728 | ppk-2  | polyphosphate kinase   | 1.55 |
| GSU1222 |        | histone deacetylase family protein                             | 1.54 |
| GSU0322 | gspK   | type II secretion system protein GspK                          | 1.54 |
| GSU1039 |        | sigma-54 dependent DNA-binding response regulator              | 1.54 |
| GSU1678 | mgtA   | cation-transport ATPase, E1-E2 family                          | 1.54 |
| GSU1376 |        | conserved hypothetical protein                                 | 1.54 |
| GSU3339 | groES  | chaperonin GroES   | 1.54 |
| GSU1637 | pyrE   | orotate phosphoribosyltransferase                              | 1.53 |
| GSU2255 |        | glycosyl transferase, putative                                 | 1.53 |
| GSU3199 | cheA-3 | chemotaxis sensor histidine kinase CheA                        | 1.53 |
| GSU1769 |        | divergent polysaccharide deacetylase domain protein            | 1.53 |
| GSU2838 | rplO   | ribosomal protein L15  | 1.52 |
| GSU1242 | aatA   | aspartate aminotransferase                                     | 1.52 |
| GSU2426 |        | mcbC-like oxidoreductase for polypeptide thioester cyclization | 1.52 |
| GSU2583 | ycaC   | isochorismatase family protein YcaC                            | 1.52 |

|         |      |  |      |
|---------|------|--|------|
| GSU3306 |      | conserved hypothetical protein   | 1.52 |
| GSU2698 |      | transcriptional regulator, TetR family                                   | 1.51 |
| GSU3367 | ispF | 2C-methyl-D-erythritol 2,4-cyclodiphosphate synthase                     | 1.51 |
| GSU0617 |      | NHL repeat domain lipoprotein  | 1.51 |
| GSU0644 |      | RNA-binding KH domain protein, putative                                  | 1.51 |
| GSU1810 | tilS | tRNA(Ile)-lysidine synthetase  | 1.51 |
| GSU0212 |      | ABC transporter, ATP-binding protein                                     | 1.50 |
| GSU2796 | etfA | electron transfer flavoprotein, alpha subunit                            | 1.50 |
| GSU0610 | purD | phosphoribosylamine--glycine ligase                                      | 1.50 |
| GSU0815 |      | ABC transporter, periplasmic substrate-binding protein, MCE family       | 1.50 |
| GSU1731 | livG | branched-chain amino acid ABC transporter, ATP-binding protein           | 1.50 |
| GSU2377 |      | conserved hypothetical protein   | 1.50 |
| GSU2616 | secF | protein-export membrane protein SecF                                     | 1.50 |
| GSU2028 | pilQ | type IV pilus biogenesis protein PilQ                                    | 1.50 |
| GSU1860 | vorB | 2-oxoacid:ferredoxin oxidoreductase, thiamin diphosphate-binding subunit | 1.50 |
| GSU2089 | mreB | rod shape-determining protein MreB                                       | 1.50 |
| GSU2875 | rpsI | ribosomal protein S9   | 1.50 |

Table B2: Proteins with lower abundance under U(VI) exposure.  $\Delta z$ -score was calculated as follows: (z-score in U treatment - z-score in control).

| Locus ID | Symbol | Name  | $\Delta z$ |
|----------|--------|---|------------|
| GSU3206  |        | zinc finger transcriptional regulator, TraR/DksA family       | -1.50      |
| GSU3314  |        | lipoprotein, putative   | -1.50      |
| GSU3207  | gpmI   | phosphoglycerate mutase, 2,3-bisphosphoglycerate-independent  | -1.50      |
| GSU0810  |        | OmpA domain protein   | -1.50      |
| GSU2359  |        | glycoside hydrolase, family 57, DUF3536 domain-containing     | -1.50      |
| GSU3062  |        | radical SAM domain iron-sulfur cluster-binding oxidoreductase | -1.50      |

|         |        |   |       |
|---------|--------|---|-------|
| GSU2861 | rpsG   | ribosomal protein S7  | -1.51 |
| GSU1725 | sbcC-2 | DNA repair exonuclease SbcCD, C subunit, putative                         | -1.51 |
| GSU1701 |        | diadenosine polyphosphate hydrolase, FHIT domain-containing               | -1.51 |
| GSU1516 | infC   | translation initiation factor IF-3  | -1.51 |
| GSU2362 |        | transcriptional regulator, MarR family                                    | -1.52 |
| GSU0547 | mutS-2 | DNA mismatch repair ATPase MutS-2   | -1.52 |
| GSU2697 | acrA   | efflux pump, RND family, membrane fusion lipoprotein                      | -1.52 |
| GSU2424 |        | conserved hypothetical protein  | -1.52 |
| GSU1061 |        | aspartate aminotransferase  | -1.53 |
| GSU2090 |        | conserved hypothetical protein  | -1.53 |
| GSU1521 | ihfA-1 | integration host factor, alpha subunit                                    | -1.53 |
| GSU2372 | mcp028 | methyl-accepting chemotaxis sensory transducer, putative                  | -1.53 |
| GSU2841 | rplR   | ribosomal protein L18   | -1.53 |
| GSU1941 |        | sensor histidine kinase, GAF domain-containing                            | -1.54 |
| GSU0782 | hybS   | periplasmically oriented, membrane-bound [NiFe]-hydrogenase small subunit | -1.54 |
| GSU2238 | gmk    | guanylate kinase  | -1.54 |
| GSU2206 | rpsT   | ribosomal protein S20   | -1.54 |
| GSU0233 |        | protein of unknown function DUF480  | -1.55 |
| GSU1636 | purF   | glutamine--phosphoribosylpyrophosphate amidotransferase                   | -1.55 |
| GSU1886 | yfiA   | ribosomal subunit interface-associated sigma-54 modulation protein        | -1.55 |
| GSU2461 |        | conserved hypothetical protein  | -1.55 |
| GSU1110 | ndk    | nucleoside diphosphate kinase   | -1.56 |
| GSU0452 |        | sensor histidine kinase   | -1.56 |
| GSU3319 | ppiA   | cytosolic peptidylprolyl cis-trans isomerase, cyclophilin A-like          | -1.56 |
| GSU0913 | uup    | DNA-binding ATPase Uup  | -1.57 |
| GSU3059 |        | radical SAM domain iron-sulfur cluster-binding oxidoreductase             | -1.57 |
| GSU0921 |        | ribonuclease, Rne/Rng family protein                                      | -1.57 |
| GSU2665 |        | efflux pump, RND family, membrane fusion lipoprotein                      | -1.57 |



|         |        |   |       |
|---------|--------|---|-------|
| GSU2004 | ubiD-2 | UbiD family decarboxylase   | -1.57 |
| GSU2846 | rplX   | ribosomal protein L24   | -1.57 |
| GSU1839 |        | phosphatase/phosphohexomutase-related hydrolase                               | -1.57 |
| GSU2853 | rpsS   | ribosomal protein S19   | -1.57 |
| GSU0023 |        | TPR domain protein  | -1.58 |
| GSU1932 |        | SPOR domain protein   | -1.58 |
| GSU1337 |        | lipoprotein, putative   | -1.58 |
| GSU1743 |        | lipoprotein, putative   | -1.58 |
| GSU0169 |        | ABC transporter, ATP-binding protein  | -1.58 |
| GSU1345 |        | transcriptional regulator, Rrf2 family  | -1.58 |
| GSU1496 | pilA   | geopilin  | -1.58 |
| GSU0108 |        | ATP synthase F0, B subunit, putative  | -1.59 |
| GSU2207 | holA   | DNA polymerase III, delta subunit   | -1.59 |
| GSU0894 |        | peptidyl-prolyl cis-trans isomerase, cyclophilin-type                         | -1.59 |
| GSU0310 |        | phospholipase, patatin family, putative                                       | -1.59 |
| GSU1469 | korB   | 2-oxoglutarate:ferredoxin oxidoreductase, thiamin diphosphate-binding subunit | -1.59 |
| GSU1861 | vorA   | 2-oxoacid:ferredoxin oxidoreductase, alpha subunit                            | -1.59 |
| GSU1873 | pepF   | oligoendopeptidase F  | -1.59 |
| GSU1479 |        | conserved hypothetical protein  | -1.60 |
| GSU2413 |        | ABC transporter, ATP-binding protein  | -1.60 |
| GSU2921 | metH   | 5-methyltetrahydrofolate--homocysteine methyltransferase                      | -1.60 |
| GSU2602 | ihfB-2 | DNA-binding protein HU  | -1.60 |
| GSU0027 |        | ExbD/TolR-related biopolymer transport membrane protein                       | -1.60 |
| GSU0145 | recA   | recA protein  | -1.60 |
| GSU0442 | mqnC-1 | dehypoxanthinylfutasine cyclase, putative                                     | -1.60 |
| GSU1594 |        | zinc-dependent peptidase, PqqL family   | -1.61 |
| GSU0771 |        | zinc-dependent oxidoreductase   | -1.61 |
| GSU2788 |        | OsmC family protein   | -1.62 |

|         |       |   |       |
|---------|-------|---|-------|
| GSU3092 | yqeY  | uncharacterized protein YqeY                            | -1.62 |
| GSU1000 |       | conserved hypothetical protein                          | -1.62 |
| GSU1868 |       | cysteine desulfurase family protein                     | -1.62 |
| GSU1790 | loN-2 | ATP-dependent protease La                               | -1.62 |
| GSU0803 | ppsA  | phosphoenolpyruvate synthase                            | -1.62 |
| GSU2087 | gmhA  | D-sedoheptulose-7-phosphate isomerase                   | -1.63 |
| GSU1319 |       | sensor histidine kinase                                 | -1.63 |
| GSU3099 | hisC  | histidinol-phosphate aminotransferase                   | -1.63 |
| GSU2973 |       | lipoprotein, putative                                   | -1.63 |
| GSU1278 |       | protein of unknown function DUF1858                     | -1.63 |
| GSU3405 |       | amino acid ABC transporter, permease protein            | -1.63 |
| GSU2248 |       | conserved hypothetical protein                          | -1.63 |
| GSU2195 | guaB  | inosine-5-monophosphate dehydrogenase                   | -1.64 |
| GSU2521 | yedF  | selenium metabolism protein YedF, putative              | -1.64 |
| GSU3111 |       | conserved hypothetical protein                          | -1.64 |
| GSU0388 |       | conserved hypothetical protein                          | -1.64 |
| GSU3132 | hup   | histone-like protein                                    | -1.64 |
| GSU0824 |       | conserved hypothetical protein                          | -1.64 |
| GSU3095 | hisF  | imidazoleglycerol phosphate synthase, cyclase subunit   | -1.64 |
| GSU1519 | pheS  | phenylalanyl-tRNA synthetase, alpha subunit             | -1.64 |
| GSU1866 |       | PhoH-related ATPase                                     | -1.65 |
| GSU2183 |       | Fic family protein                                      | -1.65 |
| GSU2074 |       | peptidylprolyl cis-trans isomerase, PpiC-type           | -1.65 |
| GSU2957 | trx-2 | thioredoxin family protein                              | -1.65 |
| GSU1920 | tsf   | translation elongation factor Ts                        | -1.65 |
| GSU2191 |       | aldehyde ferredoxin oxidoreductase, tungsten-containing | -1.65 |
| GSU2353 |       | conserved hypothetical protein                          | -1.66 |
| GSU1106 | gltA  | citrate synthase  | -1.66 |
| GSU2743 |       | cytochrome c, 1 heme-binding site                       | -1.66 |
| GSU1828 |       | chorismate mutase                                       | -1.66 |

|         |        |  |       |
|---------|--------|--|-------|
| GSU1002 |        | YcaC-related hydrolase, putative   | -1.66 |
| GSU0654 | thiF-1 | thiamin biosynthesis thiocarboxylate synthase                                  | -1.66 |
| GSU0443 |        | ribonuclease D, putative   | -1.66 |
| GSU2603 | rpsA   | ribosomal protein S1   | -1.67 |
| GSU0570 |        | SAM-dependent methyltransferase, type 11                                       | -1.67 |
| GSU1782 | pulM   | type II secretion system ATPase PulM, putative                                 | -1.67 |
| GSU1311 | pgi    | glucose-6-phosphate isomerase  | -1.67 |
| GSU1468 | korA   | 2-oxoglutarate:ferredoxin oxidoreductase, alpha subunit                        | -1.68 |
| GSU2842 | rplF   | ribosomal protein L6   | -1.69 |
| GSU2737 | OmcB   | polyheme membrane-associated cytochrome c                                      | -1.69 |
| GSU1901 |        | conserved hypothetical protein   | -1.69 |
| GSU1975 |        | NAD-dependent epimerase/dehydratase family protein                             | -1.69 |
| GSU2285 |        | membrane-associated metal-dependent phosphohydrolase, HDc domain-containing    | -1.70 |
| GSU0102 | selB   | selenocysteine-specific translation elongation factor                          | -1.70 |
| GSU1911 | ilvB   | acetolactate synthase, large subunit, biosynthetic type                        | -1.71 |
| GSU0915 |        | conserved hypothetical protein   | -1.71 |
| GSU1254 |        | hypothetical protein   | -1.71 |
| GSU2270 | lolE   | lipoprotein release ABC transporter, membrane protein                          | -1.71 |
| GSU2833 | rpsK   | ribosomal protein S11  | -1.72 |
| GSU0949 |        | efflux transporter, RND family, MFP subunit                                    | -1.72 |
| GSU0542 |        | diguanylate cyclase  | -1.73 |
| GSU0643 | rpsP   | ribosomal protein S16  | -1.73 |
| GSU1199 |        | nuclease, putative   | -1.74 |
| GSU3213 | obgE   | ribosome biogenesis GTPase ObgE  | -1.74 |
| GSU2939 |        | porin, putative  | -1.74 |
| GSU0111 | atpA   | ATP synthase F1, alpha subunit   | -1.74 |
| GSU2435 | aceF   | pyruvate dehydrogenase complex, E2 protein, dihydrolipoamide acetyltransferase | -1.74 |
| GSU1754 | kamA   | L-lysine 2,3-aminomutase   | -1.74 |

|         |        |  |       |
|---------|--------|--|-------|
| GSU1772 | ctpA-2 | periplasmic carboxy-terminal processing protease lipoprotein   | -1.75 |
| GSU2813 | ccpA   | cytochrome c peroxidase, 2 heme-binding sites                  | -1.75 |
| GSU0859 | galU   | UTP-glucose-1-phosphate uridylyltransferase                    | -1.75 |
| GSU3190 |        | twin-arginine translocation protein, TatA/E family             | -1.75 |
| GSU1304 | mcp025 | methyl-accepting chemotaxis sensory transducer                 | -1.75 |
| GSU2360 |        | maltooligosyltrehalose synthase, putative                      | -1.76 |
| GSU1609 |        | efflux pump, RND family, outer membrane protein                | -1.76 |
| GSU2273 |        | conserved hypothetical protein                                 | -1.76 |
| GSU0115 | pdxA   | 4-hydroxythreonine-4-phosphate dehydrogenase                   | -1.76 |
| GSU3139 |        | protein of unknown function DUF399                             | -1.76 |
| GSU0816 |        | organic solvent tolerance ABC transporter, ATP-binding protein | -1.76 |
| GSU0355 |        | conserved hypothetical protein                                 | -1.76 |
| GSU1321 | trx-1  | TlpA family-related protein disulfide reductase lipoprotein    | -1.76 |
| GSU3376 |        | response receiver-modulated diguanylate cyclase                | -1.77 |
| GSU0488 | trxB   | thioredoxin reductase  | -1.78 |
| GSU0376 | gcvH-1 | glycine cleavage system H protein                              | -1.78 |
| GSU1802 | yjeF   | YjeF-related putative carbohydrate kinase                      | -1.78 |
| GSU3194 | thiL   | thiamine monophosphate kinase                                  | -1.79 |
| GSU3013 | engB   | GTPase EngB  | -1.79 |
| GSU1060 |        | conserved hypothetical protein                                 | -1.79 |
| GSU1844 |        | IPT/TIG domain protein, putative                               | -1.79 |
| GSU2184 | ccaC   | cytidine-specific tRNA nucleotidyltransferase                  | -1.79 |
| GSU2019 | accC   | acetyl-CoA carboxylase, biotin carboxylase                     | -1.80 |
| GSU1981 |        | conserved hypothetical protein                                 | -1.80 |
| GSU2502 |        | spermine/spermidine synthase family protein                    | -1.80 |
| GSU2335 | usp-4  | universal stress protein Usp                                   | -1.81 |
| GSU2835 | map    | methionine aminopeptidase, type I                              | -1.81 |
| GSU2187 |        | ABC transporter, permease protein                              | -1.81 |

Table B3:  $\Delta z$ -score of proteins involved in protein fate.  $\Delta z$ -score was calculated as follows: (z-score in U treatment - z-score in control).

| Locus ID | Symbol | Name   | Category   | $\Delta z$ |
|----------|--------|--|--|------------|
| GSU2869  | secE   | preprotein translocase, SecE subunit                 | Protein fate, Protein and peptide secretion and trafficking        | 1.73       |
| GSU1778  | pulQ   | type II secretion system secretin lipoprotein PulQ   | Protein fate, Protein and peptide secretion and trafficking        | 1.65       |
| GSU0032  | grpE   | DnaJ adenine nucleotide exchange factor GrpE         | Protein fate, Protein folding and stabilization                    | 1.63       |
| GSU0322  | gspK   | type II secretion system protein GspK                | Protein fate, Protein and peptide secretion and trafficking        | 1.54       |
| GSU3339  | groES  | chaperonin GroES                                     | Protein fate, Protein folding and stabilization                    | 1.54       |
| GSU2616  | secF   | protein-export membrane protein SecF                 | Protein fate, Protein and peptide secretion and trafficking        | 1.50       |
| GSU2433  |        | ATP-dependent protease, putative                     | Protein fate, Degradation of proteins, peptides, and glycopeptides | 1.48       |
| GSU2410  |        | heat shock protein, Hsp20 family                     | Protein fate, Protein folding and stabilization                    | 1.43       |
| GSU2075  |        | subtilisin   | Protein fate, Degradation of proteins, peptides, and glycopeptides | 1.42       |
| GSU1865  |        | metalloendopeptidase, putative, glycoprotease family | Protein fate, Degradation of proteins, peptides, and               | 1.29       |

|         |        |   |  |      |
|---------|--------|---|--|------|
|         |        |   | glycopeptides  |      |
| GSU1791 | clpX   | ATP-dependent Clp protease,<br>ATP-binding subunit ClpX | Protein fate, Degradation<br>of proteins, peptides, and<br>glycopeptides | 1.26 |
| GSU1627 | secG   | preprotein translocase, SecG<br>subunit                 | Protein fate, Protein and<br>peptide secretion and<br>trafficking        | 1.22 |
| GSU2617 | secD   | protein-export membrane protein<br>SecD                 | Protein fate, Protein and<br>peptide secretion and<br>trafficking        | 1.12 |
| GSU1437 |        | peptidase, M48 family                                   | Protein fate, Degradation<br>of proteins, peptides, and<br>glycopeptides | 1.12 |
| GSU2021 | pepQ-2 | xaa-pro dipeptidase                                     | Protein fate, Degradation<br>of proteins, peptides, and<br>glycopeptides | 1.12 |
| GSU1792 | clpP   | ATP-dependent Clp protease,<br>proteolytic subunit ClpP | Protein fate, Degradation<br>of proteins, peptides, and<br>glycopeptides | 1.10 |
| GSU0969 | ctpA-1 | carboxy-terminal processing<br>protease                 | Protein fate, Degradation<br>of proteins, peptides, and<br>glycopeptides | 1.05 |
| GSU0823 | ppiC   | peptidyl-prolyl cis-trans isomerase<br>C                | Protein fate, Protein<br>folding and stabilization                       | 1.04 |
| GSU3348 |        | chaperonin, 33 kDa family                               | Protein fate, Protein<br>folding and stabilization                       | 0.95 |
| GSU2060 |        | pmbA protein, putative                                  | Protein fate, Protein<br>modification and repair                         | 0.91 |
| GSU2390 | htpG   | heat shock protein HtpG                                 | Protein fate, Protein<br>folding and stabilization                       | 0.90 |

|         |       |  |  |      |
|---------|-------|--|--|------|
| GSU0928 |       | peptidase, M16 family                                    | Protein fate, Degradation of proteins, peptides, and glycopeptides | 0.90 |
| GSU0332 | pepA  | aminopeptidase A/I                                       | Protein fate, Degradation of proteins, peptides, and glycopeptides | 0.75 |
| GSU0321 |       | general secretion pathway protein L, putative            | Protein fate, Protein and peptide secretion and trafficking        | 0.68 |
| GSU0328 | gspE  | general secretion pathway protein E                      | Protein fate, Protein and peptide secretion and trafficking        | 0.68 |
| GSU0080 | degQ  | protease degQ  | Protein fate, Degradation of proteins, peptides, and glycopeptides | 0.57 |
| GSU1132 | ftsY  | signal recognition particle-docking protein FtsY         | Protein fate, Protein and peptide secretion and trafficking        | 0.56 |
| GSU0330 |       | general secretion pathway protein C, putative            | Protein fate, Protein and peptide secretion and trafficking        | 0.52 |
| GSU0228 |       | peptidyl-prolyl cis-trans isomerase, FKBP-type, putative | Protein fate, Protein folding and stabilization                    | 0.40 |
| GSU0129 | def-1 | polypeptide deformylase                                  | Protein fate, Protein modification and repair                      | 0.28 |
| GSU3135 | lspA  | signal peptidase II                                      | Protein fate, Protein and peptide secretion and trafficking        | 0.26 |
| GSU0306 | hypF  | hydrogenase maturation protein HypF                      | Protein fate, Protein modification and repair                      | 0.25 |
| GSU2618 |       | preprotein translocase, YajC                             | Protein fate, Protein and  | 0.21 |

|         |       |  |  |       |
|---------|-------|--|--|-------|
|         |       | subunit  | peptide secretion and trafficking                                  |       |
| GSU3193 | loN-3 | ATP-dependent protease La                          | Protein fate, Degradation of proteins, peptides, and glycopeptides | 0.12  |
| GSU1914 |       | membrane-associated zinc metalloprotease, putative | Protein fate, Degradation of proteins, peptides, and glycopeptides | 0.09  |
| GSU2837 | secY  | preprotein translocase, SecY subunit               | Protein fate, Protein and peptide secretion and trafficking        | 0.05  |
| GSU0383 |       | peptidyl-prolyl cis-trans isomerase, FKBP-type     | Protein fate, Protein folding and stabilization                    | 0.01  |
| GSU0923 | loN-1 | ATP-dependent protease La                          | Protein fate, Degradation of proteins, peptides, and glycopeptides | -0.11 |
| GSU0305 | hypB  | hydrogenase accessory protein HypB                 | Protein fate, Protein folding and stabilization                    | -0.14 |
| GSU2050 | secA  | preprotein translocase, SecA subunit               | Protein fate, Protein and peptide secretion and trafficking        | -0.40 |
| GSU2823 |       | HlyD family secretion protein                      | Protein fate, Protein and peptide secretion and trafficking        | -0.51 |
| GSU1267 | lepB  | signal peptidase I                                 | Protein fate, Protein and peptide secretion and trafficking        | -0.52 |
| GSU1524 | pcM   | protein-L-isoaspartate O-methyltransferase         | Protein fate, Protein modification and repair                      | -0.61 |
| GSU0304 | pepN  | aminopeptidase N                                   | Protein fate, Degradation of proteins, peptides, and               | -0.64 |



|         |       |   |  |       |
|---------|-------|---|--|-------|
|         |       |   | glycopeptides  |       |
| GSU0034 | dnaJ  | chaperone protein dnaJ                                    | Protein fate, Protein folding and stabilization                    | -1.07 |
| GSU1610 |       | efflux transporter, RND family, MFP subunit               | Protein fate, Protein and peptide secretion and trafficking        | -1.08 |
| GSU0927 |       | peptidase, M16 family                                     | Protein fate, Degradation of proteins, peptides, and glycopeptides | -1.08 |
| GSU0658 | clpB  | ClpB protein  | Protein fate, Degradation of proteins, peptides, and glycopeptides | -1.14 |
| GSU0856 |       | peptidase, M48 family                                     | Protein fate, Degradation of proteins, peptides, and glycopeptides | -1.16 |
| GSU0308 | hypD  | hydrogenase expression/formation protein HypD             | Protein fate, Protein folding and stabilization                    | -1.21 |
| GSU0538 |       | heat shock protein, Hsp20 family                          | Protein fate, Protein folding and stabilization                    | -1.22 |
| GSU0642 | ffH   | signal recognition particle protein                       | Protein fate, Protein and peptide secretion and trafficking        | -1.23 |
| GSU3203 |       | outer membrane lipoprotein carrier protein LolA, putative | Protein fate, Protein and peptide secretion and trafficking        | -1.24 |
| GSU3456 | def-2 | polypeptide deformylase                                   | Protein fate, Protein modification and repair                      | -1.24 |
| GSU1793 | tig   | trigger factor  | Protein fate, Protein and peptide secretion and trafficking        | -1.30 |

|         |        |  |  |       |
|---------|--------|--|--|-------|
| GSU0786 |        | hydrogenase maturation protease                                  | Protein fate, Protein modification and repair                      | -1.34 |
| GSU3340 | groEL  | 60 kDa chaperonin  | Protein fate, Protein folding and stabilization                    | -1.35 |
| GSU3347 |        | peptidase, U32 family  | Protein fate, Degradation of proteins, peptides, and glycopeptides | -1.38 |
| GSU1105 | pepQ-1 | xaa-pro dipeptidase  | Protein fate, Degradation of proteins, peptides, and glycopeptides | -1.44 |
| GSU0033 | dnaK   | chaperone protein dnaK   | Protein fate, Protein folding and stabilization                    | -1.45 |
| GSU0329 |        | general secretion pathway protein D, putative                    | Protein fate, Protein and peptide secretion and trafficking        | -1.48 |
| GSU3319 | ppiA   | cytosolic peptidylprolyl cis-trans isomerase, cyclophilin A-like | Protein fate, Protein folding and stabilization                    | -1.56 |
| GSU0894 |        | peptidyl-prolyl cis-trans isomerase, cyclophilin-type            | Protein fate, Protein folding and stabilization                    | -1.59 |
| GSU1873 | pepF   | oligoendopeptidase F   | Protein fate, Degradation of proteins, peptides, and glycopeptides | -1.59 |
| GSU1594 |        | zinc-dependent peptidase, PqqL family                            | Protein fate, Degradation of proteins, peptides, and glycopeptides | -1.61 |
| GSU1790 | loN-2  | ATP-dependent protease La  | Protein fate, Degradation of proteins, peptides, and glycopeptides | -1.62 |
| GSU1772 | ctpA-2 | periplasmic carboxy-terminal processing protease lipoprotein     | Protein fate, Degradation of proteins, peptides, and glycopeptides | -1.75 |

|         |     |  |   |       |
|---------|-----|--|---|-------|
| GSU3190 |     | twin-arginine translocation protein, TatA/E family | Protein fate, Protein and peptide secretion and trafficking | -1.75 |
| GSU2835 | map | methionine aminopeptidase, type I                  | Protein fate, Protein modification and repair               | -1.81 |

Table B4:  $\Delta z$ -score of proteins involved in nucleotide and nucleoside metabolism.  $\Delta z$ -score was calculated as follows: (z-score in U treatment - z-score in control)

| Locus ID | Symbol | Name                              | Category   | $\Delta z$ |
|----------|--------|-----------------------------------|--|------------|
| GSU1919  | pyrH   | uridylate kinase                  | Purines, pyrimidines, nucleosides, and nucleotides, Nucleotide and nucleoside interconversions | 1.79       |
| GSU0483  | queC   | 7-cyano-7-deazaguanine synthase   | Purines, pyrimidines, nucleosides, and nucleotides   | 1.73       |
| GSU0933  | upp    | uracil phosphoribosyltransferase  | Purines, pyrimidines, nucleosides, and nucleotides, Salvage of nucleosides and nucleotides     | 1.60       |
| GSU1632  | purB   | adenylosuccinate lyase            | Purines, pyrimidines, nucleosides, and nucleotides, Purine ribonucleotide biosynthesis         | 1.57       |
| GSU1637  | pyrE   | orotate phosphoribosyltransferase | Purines, pyrimidines, nucleosides, and nucleotides, Pyrimidine ribonucleotide biosynthesis     | 1.53       |

|         |      |   |  |      |
|---------|------|---|--|------|
| GSU0610 | purD | phosphoribosylamine--glycine ligase                               | Purines, pyrimidines, nucleosides, and nucleotides, Purine ribonucleotide biosynthesis         | 1.50 |
| GSU3308 | purA | adenylosuccinate synthetase                                       | Purines, pyrimidines, nucleosides, and nucleotides, Purine ribonucleotide biosynthesis         | 1.41 |
| GSU2091 | purC | phosphoribosylaminoimidazole-succinocarboxamide synthase          | Purines, pyrimidines, nucleosides, and nucleotides, Purine ribonucleotide biosynthesis         | 1.40 |
| GSU1272 | pyrC | dihydroorotase, multifunctional complex type                      | Purines, pyrimidines, nucleosides, and nucleotides, Pyrimidine ribonucleotide biosynthesis     | 1.32 |
| GSU2605 | cmk  | cytidylate kinase   | Purines, pyrimidines, nucleosides, and nucleotides, Nucleotide and nucleoside interconversions | 1.26 |
| GSU3058 |      | dihydroorotate dehydrogenase, electron transfer subunit, putative | Purines, pyrimidines, nucleosides, and nucleotides, Pyrimidine ribonucleotide biosynthesis     | 1.18 |
| GSU1756 |      | dihydroorotate dehydrogenase, electron transfer subunit, putative | Purines, pyrimidines, nucleosides, and nucleotides, Pyrimidine ribonucleotide biosynthesis     | 1.16 |
| GSU1526 | apt  | adenine phosphoribosyltransferase                                 | Purines, pyrimidines, nucleosides, and   | 1.11 |

|         |        |  |  |      |
|---------|--------|--|--|------|
|         |        |  | nucleotides, Salvage of nucleosides and nucleotides  |      |
| GSU3106 | thyX   | thymidylate synthase, flavin-dependent                                       | Purines, pyrimidines, nucleosides, and nucleotides, 2'-Deoxyribonucleotide metabolism      | 0.88 |
| GSU1271 | pyrB   | aspartate carbamoyltransferase   | Purines, pyrimidines, nucleosides, and nucleotides, Pyrimidine ribonucleotide biosynthesis | 0.83 |
| GSU1755 | pyrD   | dihydroorotate dehydrogenase   | Purines, pyrimidines, nucleosides, and nucleotides, Pyrimidine ribonucleotide biosynthesis | 0.41 |
| GSU0611 | purE-1 | phosphoribosylaminoimidazole carboxylase, catalytic subunit                  | Purines, pyrimidines, nucleosides, and nucleotides, Purine ribonucleotide biosynthesis     | 0.26 |
| GSU2194 | guaA   | GMP synthase   | Purines, pyrimidines, nucleosides, and nucleotides, Purine ribonucleotide biosynthesis     | 0.18 |
| GSU0609 | purH   | phosphoribosylaminoimidazolecarboxamide formyltransferase/IMP cyclohydrolase | Purines, pyrimidines, nucleosides, and nucleotides, Purine ribonucleotide biosynthesis     | 0.18 |
| GSU1634 |        | phosphoribosylformylglycinamide synthase II, putative                        | Purines, pyrimidines, nucleosides, and nucleotides, Purine                                 | 0.06 |

|         |      |  |  |       |
|---------|------|--|--|-------|
|         |      |  | ribonucleotide biosynthesis  |       |
| GSU1112 | mtaP | methylthioadenosine phosphorylase                | Purines, pyrimidines, nucleosides, and nucleotides, Salvage of nucleosides and nucleotides | 0.05  |
| GSU1017 |      | hypoxanthine phosphoribosyltransferase, putative | Purines, pyrimidines, nucleosides, and nucleotides, Salvage of nucleosides and nucleotides | 0.04  |
| GSU1895 | pyrG | CTP synthase                                     | Purines, pyrimidines, nucleosides, and nucleotides, Pyrimidine ribonucleotide biosynthesis | -0.16 |
| GSU1273 | carA | carbamoyl-phosphate synthase, small subunit      | Purines, pyrimidines, nucleosides, and nucleotides, Pyrimidine ribonucleotide biosynthesis | -0.31 |
| GSU1276 | carB | carbamoyl-phosphate synthase, large subunit      | Purines, pyrimidines, nucleosides, and nucleotides, Pyrimidine ribonucleotide biosynthesis | -0.45 |
| GSU1461 | pyrF | orotidine 5'-phosphate decarboxylase             | Purines, pyrimidines, nucleosides, and nucleotides, Pyrimidine ribonucleotide biosynthesis | -0.47 |
| GSU1759 | purN | phosphoribosylglycinamide formyltransferase      | Purines, pyrimidines, nucleosides, and nucleotides, Purine ribonucleotide biosynthesis     | -0.48 |

|         |        |   |  |       |
|---------|--------|---|--|-------|
| GSU1758 | purM   | phosphoribosylformylglycinamide cyclo-ligase                | Purines, pyrimidines, nucleosides, and nucleotides, Purine ribonucleotide biosynthesis         | -0.93 |
| GSU1871 |        | ribonucleoside-diphosphate reductase, putative              | Purines, pyrimidines, nucleosides, and nucleotides, 2'-Deoxyribonucleotide metabolism          | -1.08 |
| GSU2306 | purE-2 | phosphoribosylaminoimidazole carboxylase, catalytic subunit | Purines, pyrimidines, nucleosides, and nucleotides, Purine ribonucleotide biosynthesis         | -1.27 |
| GSU1635 |        | phosphoribosylformylglycinamide synthase I, putative        | Purines, pyrimidines, nucleosides, and nucleotides, Purine ribonucleotide biosynthesis         | -1.32 |
| GSU2836 | adk    | adenylate kinase  | Purines, pyrimidines, nucleosides, and nucleotides, Nucleotide and nucleoside interconversions | -1.40 |
| GSU0661 | prsA   | ribose-phosphate pyrophosphokinase                          | Purines, pyrimidines, nucleosides, and nucleotides, Purine ribonucleotide biosynthesis         | -1.49 |
| GSU2238 | gmk    | guanylate kinase  | Purines, pyrimidines, nucleosides, and nucleotides, Nucleotide and nucleoside interconversions | -1.54 |

|         |      |  |  |       |
|---------|------|--|--|-------|
| GSU1636 | purF | glutamine--<br>phosphoribosylpyrophosphate<br>amidotransferase | Purines, pyrimidines,<br>nucleosides, and<br>nucleotides, Purine<br>ribonucleotide biosynthesis            | -1.55 |
| GSU1110 | ndk  | nucleoside diphosphate kinase                                  | Purines, pyrimidines,<br>nucleosides, and<br>nucleotides, Nucleotide<br>and nucleoside<br>interconversions | -1.56 |
| GSU2195 | guaB | inosine-5-monophosphate<br>dehydrogenase                       | Purines, pyrimidines,<br>nucleosides, and<br>nucleotides, Purine<br>ribonucleotide biosynthesis            | -1.64 |

Table B5:  $\Delta z$ -score of proteins involved in biosynthesis of cofactors.  $\Delta z$ -score was calculated as follows: (z-score in U treatment - z-score in control)

| Locus ID | Symbol | Name   | Category  | Dz   |
|----------|--------|--|---|------|
| GSU1459  | ispG   | 4-hydroxy-3-methylbut-2-en-1-yl<br>diphosphate synthase    | Biosynthesis of cofactors,<br>prosthetic groups, and<br>carriers, Other                   | 1.71 |
| GSU1827  | nadB   | L-aspartate oxidase  | Biosynthesis of cofactors,<br>prosthetic groups, and<br>carriers, Pyridine<br>nucleotides | 1.71 |
| GSU1942  | capL   | UDP-N-acetyl-D-galactosamine 6-<br>dehydrogenase, putative | Biosynthesis and<br>degradation of surface<br>polysaccharides and<br>lipopolysaccharides  | 1.67 |
| GSU1706  | panC   | pantoate--beta-alanine ligase                              | Biosynthesis of cofactors,<br>prosthetic groups, and<br>carriers, Pantothenate and        | 1.66 |



|         |        |  |  |      |
|---------|--------|--|--|------|
|         |        |  | coenzyme A   |      |
| GSU0867 | ubiE   | ubiquinone/menaquinone biosynthesis methyltransferase<br>UbiE, putative        | Biosynthesis of cofactors, prosthetic groups, and carriers, Menaquinone and ubiquinone     | 1.65 |
| GSU1584 | bioB   | biotin synthetase  | Biosynthesis of cofactors, prosthetic groups, and carriers, Biotin                         | 1.64 |
| GSU3010 | cobU   | adenosylcobinamide kinase and adenosylcobinamide phosphate guanylyltransferase | Biosynthesis of cofactors, prosthetic groups, and carriers, Heme, porphyrin, and cobalamin | 1.62 |
| GSU0604 | thiC-1 | 4-amino-5-hydroxymethyl-2-methylpyrimidine synthetase                          | Biosynthesis of cofactors, prosthetic groups, and carriers, Thiamine                       | 1.61 |
| GSU2051 | paaK-3 | phenylacetate-coenzyme A ligase  | Biosynthesis of cofactors, prosthetic groups, and carriers, Menaquinone and ubiquinone     | 1.60 |
| GSU3367 | ispF   | 2C-methyl-D-erythritol 2,4-cyclodiphosphate synthase                           | Biosynthesis of cofactors, prosthetic groups, and carriers, Other                          | 1.51 |
| GSU1577 | cobO   | cob(I)alamin adenosyltransferase   | Biosynthesis of cofactors, prosthetic groups, and carriers, Heme, porphyrin, and cobalamin | 1.49 |
| GSU0588 | thiG   | thiamine biosynthesis protein<br>ThiG  | Biosynthesis of cofactors, prosthetic groups, and carriers, Thiamine                       | 1.43 |
| GSU1691 | ribE   | 6,7-dimethyl-8-ribityllumazine synthase  | Biosynthesis of cofactors, prosthetic groups, and  | 1.41 |

|         |      |  |  |      |
|---------|------|--|--|------|
|         |      |  | carriers, Riboflavin, FMN, and FAD   |      |
| GSU2264 | lpxA | acyl-(acyl-carrier-protein)--UDP-N-acetylglucosamine O-acyltransferase | Biosynthesis and degradation of surface polysaccharides and lipopolysaccharides            | 1.40 |
| GSU2289 |      | nicotinate phosphoribosyltransferase, putative                         | Biosynthesis of cofactors, prosthetic groups, and carriers, Pyridine nucleotides           | 1.31 |
| GSU2995 | cobI | precorrin-2 C20-methyltransferase                                      | Biosynthesis of cofactors, prosthetic groups, and carriers, Heme, porphyrin, and cobalamin | 1.31 |
| GSU2241 |      | capsular polysaccharide biosynthesis protein I                         | Biosynthesis and degradation of surface polysaccharides and lipopolysaccharides            | 1.25 |
| GSU2011 |      | cysteine desulfurase   | Biosynthesis of cofactors, prosthetic groups, and carriers, Other                          | 1.18 |
| GSU1815 |      | NAD-dependent epimerase/dehydratase family protein                     | Biosynthesis and degradation of surface polysaccharides and lipopolysaccharides            | 1.17 |
| GSU2256 |      | ADP-heptose--LPS heptosyltransferase II, putative                      | Biosynthesis and degradation of surface polysaccharides and lipopolysaccharides            | 1.13 |
| GSU0021 | nadA | quinolinate synthetase complex, subunit A                              | Biosynthesis of cofactors, prosthetic groups, and  | 1.06 |

|         |       |  |  |      |
|---------|-------|--|--|------|
|         |       |  | carriers, Pyridine nucleotides   |      |
| GSU2261 | lpxB  | lipid A disaccharide synthase (lpxB)                   | Biosynthesis and degradation of surface polysaccharides and lipopolysaccharides            | 1.01 |
| GSU2996 | cobL  | precorrin-6y c5,15-methyltransferase                   | Biosynthesis of cofactors, prosthetic groups, and carriers, Heme, porphyrin, and cobalamin | 0.98 |
| GSU0135 | hemB  | delta-aminolevulinic acid dehydratase                  | Biosynthesis of cofactors, prosthetic groups, and carriers, Heme, porphyrin, and cobalamin | 0.97 |
| GSU0660 | ispE  | 4-diphosphocytidyl-2C-methyl-D-erythritol kinase       | Biosynthesis of cofactors, prosthetic groups, and carriers, Other                          | 0.95 |
| GSU1243 | coaD  | pantetheine-phosphate adenylyltransferase              | Biosynthesis of cofactors, prosthetic groups, and carriers, Pantothenate and coenzyme A    | 0.95 |
| GSU1764 | dxs-2 | deoxyxylulose-5-phosphate synthase                     | Biosynthesis of cofactors, prosthetic groups, and carriers, Other                          | 0.93 |
| GSU1720 |       | 6-pyruvoyl tetrahydrobiopterin synthase family protein | Biosynthesis of cofactors, prosthetic groups, and carriers, Other                          | 0.91 |
| GSU0337 | hemL  | glutamate-1-semialdehyde-2,1-aminomutase               | Biosynthesis of cofactors, prosthetic groups, and carriers, Heme, porphyrin, and cobalamin | 0.88 |

|         |        |  |   |      |
|---------|--------|--|---|------|
| GSU1896 | kdsB   | 3-deoxy-D-manno-octulosonate<br>cytidyltransferase                                       | Biosynthesis and<br>degradation of surface<br>polysaccharides and<br>lipopolysaccharides            | 0.84 |
| GSU3460 |        | glycosyl transferase, group 2<br>family protein  | Biosynthesis and<br>degradation of surface<br>polysaccharides and<br>lipopolysaccharides            | 0.79 |
| GSU0012 | hemG   | protoporphyrinogen oxidase   | Biosynthesis of cofactors,<br>prosthetic groups, and<br>carriers, Heme, porphyrin,<br>and cobalamin | 0.79 |
| GSU1804 | pdxJ   | pyridoxal phosphate biosynthetic<br>protein PdxJ   | Biosynthesis of cofactors,<br>prosthetic groups, and<br>carriers, Pyridoxine                        | 0.75 |
| GSU1202 |        | mannose-1-phosphate<br>guanylyltransferase/mannose-6-<br>phosphate isomerase, truncation | Biosynthesis and<br>degradation of surface<br>polysaccharides and<br>lipopolysaccharides            | 0.73 |
| GSU1915 | dxr    | 1-deoxy-D-xylulose 5-phosphate<br>reductoisomerase                                       | Biosynthesis of cofactors,<br>prosthetic groups, and<br>carriers, Other                             | 0.66 |
| GSU0862 | fold-2 | fold bifunctional protein  | Biosynthesis of cofactors,<br>prosthetic groups, and<br>carriers, Folic acid                        | 0.66 |
| GSU2705 | moaB   | molybdenum cofactor biosynthesis<br>protein B  | Biosynthesis of cofactors,<br>prosthetic groups, and<br>carriers, Molybdopterin                     | 0.65 |
| GSU1317 | ispB   | octaprenyl-diphosphate synthase  | Biosynthesis of cofactors,<br>prosthetic groups, and<br>carriers, Menaquinone and                   | 0.60 |

|         |      |   |   |      |
|---------|------|---|---|------|
|         |      |   | ubiquinone  |      |
| GSU0440 |      | 3-octaprenyl-4-hydroxybenzoate<br>carboxy-lyase, putative | Biosynthesis of cofactors,<br>prosthetic groups, and<br>carriers, Menaquinone and<br>ubiquinone     | 0.57 |
| GSU2254 |      | glycosyl transferase, group 2<br>family protein           | Biosynthesis and<br>degradation of surface<br>polysaccharides and<br>lipopolysaccharides            | 0.46 |
| GSU0626 | gmd  | GDP-mannose 4,6-dehydratase                               | Biosynthesis and<br>degradation of surface<br>polysaccharides and<br>lipopolysaccharides            | 0.46 |
| GSU3286 |      | uroporphyrinogen III<br>synthase/methyltransferase        | Biosynthesis of cofactors,<br>prosthetic groups, and<br>carriers, Heme, porphyrin,<br>and cobalamin | 0.43 |
| GSU3285 | hemC | porphobilinogen deaminase                                 | Biosynthesis of cofactors,<br>prosthetic groups, and<br>carriers, Heme, porphyrin,<br>and cobalamin | 0.20 |
| GSU3453 | hemE | uroporphyrinogen decarboxylase                            | Biosynthesis of cofactors,<br>prosthetic groups, and<br>carriers, Heme, porphyrin,<br>and cobalamin | 0.20 |
| GSU1894 | kdsA | 2-dehydro-3-<br>deoxyphosphooctonate aldolase             | Biosynthesis and<br>degradation of surface<br>polysaccharides and<br>lipopolysaccharides            | 0.06 |
| GSU1681 |      | cobyrinic acid a,c-diamide<br>synthase family protein     | Biosynthesis of cofactors,<br>prosthetic groups, and  | 0.05 |

|         |       |  |  |       |
|---------|-------|--|--|-------|
|         |       |  | carriers, Heme, porphyrin, and cobalamin   |       |
| GSU1124 | coaBC | phosphopantothenoylcysteine decarboxylase/phosphopantothenate--cysteine ligase | Biosynthesis of cofactors, prosthetic groups, and carriers, Pantothenate and coenzyme A    | -0.02 |
| GSU1977 |       | glycosyl transferase, group 2 family protein                                   | Biosynthesis and degradation of surface polysaccharides and lipopolysaccharides            | -0.05 |
| GSU1970 |       | polysaccharide biosynthesis protein, putative                                  | Biosynthesis and degradation of surface polysaccharides and lipopolysaccharides            | -0.05 |
| GSU3368 | ispD  | 4-diphosphocytidyl-2C-methyl-D-erythritol synthase                             | Biosynthesis of cofactors, prosthetic groups, and carriers, Other                          | -0.10 |
| GSU0885 |       | cobyrinic acid a,c-diamide synthase family protein                             | Biosynthesis of cofactors, prosthetic groups, and carriers, Heme, porphyrin, and cobalamin | -0.10 |
| GSU3284 | hemA  | glutamyl-tRNA reductase  | Biosynthesis of cofactors, prosthetic groups, and carriers, Heme, porphyrin, and cobalamin | -0.11 |
| GSU2992 | cobJQ | precorrin-3B C17-methyltransferase/cobyrinic acid synthase                     | Biosynthesis of cofactors, prosthetic groups, and carriers, Heme, porphyrin, and cobalamin | -0.17 |
| GSU0999 |       | acyl-(acyl-carrier-protein)--UDP-N-acetylglucosamine O-                        | Biosynthesis and degradation of surface  | -0.26 |

|         |        |  |  |       |
|---------|--------|--|--|-------|
|         |        | acyltransferase, putative  | polysaccharides and lipopolysaccharides  |       |
| GSU3009 | cobT   | nicotinate-nucleotide--dimethylbenzimidazole phosphoribosyltransferase | Biosynthesis of cofactors, prosthetic groups, and carriers, Heme, porphyrin, and cobalamin | -0.35 |
| GSU3312 | hemH   | ferrochelatase   | Biosynthesis of cofactors, prosthetic groups, and carriers, Heme, porphyrin, and cobalamin | -0.36 |
| GSU2259 |        | 3-deoxy-D-manno-octulosonic-acid transferase, putative                 | Biosynthesis and degradation of surface polysaccharides and lipopolysaccharides            | -0.42 |
| GSU2083 | rfaA   | glucose-1-phosphate thymidyltransferase                                | Biosynthesis and degradation of surface polysaccharides and lipopolysaccharides            | -0.49 |
| GSU3006 | cobB   | cobyrinic acid a,c-diamide synthase                                    | Biosynthesis of cofactors, prosthetic groups, and carriers, Heme, porphyrin, and cobalamin | -0.49 |
| GSU0686 | dxs-1  | deoxyxylulose-5-phosphate synthase                                     | Biosynthesis of cofactors, prosthetic groups, and carriers, Other                          | -0.49 |
| GSU2704 | moaC   | molybdenum cofactor biosynthesis protein MoaC                          | Biosynthesis of cofactors, prosthetic groups, and carriers, Molybdopterin                  | -0.68 |
| GSU3005 | thiC-2 | thiamine biosynthesis protein ThiC                                     | Biosynthesis of cofactors, prosthetic groups, and carriers, Thiamine                       | -0.70 |

|         |      |   |  |       |
|---------|------|---|--|-------|
| GSU1985 |      | outer membrane protein, putative                                    | Biosynthesis and degradation of surface polysaccharides and lipopolysaccharides      | -0.70 |
| GSU1816 | ugd  | UDP-glucose 6-dehydrogenase   | Biosynthesis and degradation of surface polysaccharides and lipopolysaccharides      | -0.70 |
| GSU1854 |      | UDP-glucose/GDP-mannose dehydrogenase family protein                | Biosynthesis and degradation of surface polysaccharides and lipopolysaccharides      | -0.78 |
| GSU2337 |      | glycosyl transferase, group 20 family protein                       | Biosynthesis and degradation of surface polysaccharides and lipopolysaccharides      | -0.81 |
| GSU1690 | ribA | 3,4-dihydroxy-2-butanone 4-phosphate synthase/GTP cyclohydrolase II | Biosynthesis of cofactors, prosthetic groups, and carriers, Riboflavin, FMN, and FAD | -0.82 |
| GSU2243 |      | UDP-N-acetylglucosamine 2-epimerase                                 | Biosynthesis and degradation of surface polysaccharides and lipopolysaccharides      | -0.83 |
| GSU2570 |      | cysteine desulfurase  | Biosynthesis of cofactors, prosthetic groups, and carriers, Other                    | -0.83 |
| GSU2085 |      | ADP-heptose synthase  | Biosynthesis and degradation of surface polysaccharides and lipopolysaccharides      | -0.89 |



|         |      |  |   |       |
|---------|------|--|---|-------|
| GSU1484 |      | soluble lytic murein<br>transglycosylase, putative                         | Biosynthesis and<br>degradation of surface<br>polysaccharides and<br>lipopolysaccharides            | -0.96 |
| GSU0605 |      | thiamine-phosphate<br>pyrophosphorylase/phosphomethyl<br>pyrimidine kinase | Biosynthesis of cofactors,<br>prosthetic groups, and<br>carriers, Thiamine                          | -0.98 |
| GSU0074 | elbB | enhancing lycopene biosynthesis<br>protein 2                               | Biosynthesis of cofactors,<br>prosthetic groups, and<br>carriers, Other                             | -1.02 |
| GSU0652 | nadE | NAD <sup>+</sup> synthetase  | Biosynthesis of cofactors,<br>prosthetic groups, and<br>carriers, Pyridine<br>nucleotides           | -1.06 |
| GSU1983 |      | polysaccharide biosynthesis<br>protein, putative                           | Biosynthesis and<br>degradation of surface<br>polysaccharides and<br>lipopolysaccharides            | -1.07 |
| GSU1088 |      | ubiquinone biosynthesis protein<br>AarF, putative                          | Biosynthesis of cofactors,<br>prosthetic groups, and<br>carriers, Menaquinone and<br>ubiquinone     | -1.09 |
| GSU2999 | cobH | precorrin-8X methylmutase  | Biosynthesis of cofactors,<br>prosthetic groups, and<br>carriers, Heme, porphyrin,<br>and cobalamin | -1.10 |
| GSU3023 |      | glycosyl transferase, group 1/2<br>family protein                          | Biosynthesis and<br>degradation of surface<br>polysaccharides and<br>lipopolysaccharides            | -1.16 |
| GSU3004 |      | cobalamin biosynthesis protein   | Biosynthesis of cofactors,  | -1.21 |

|         |        |  |  |       |
|---------|--------|--|--|-------|
|         |        | CbiM   | prosthetic groups, and carriers, Heme, porphyrin, and cobalamin                        |       |
| GSU1936 | nadC   | nicotinate-nucleotide pyrophosphorylase                  | Biosynthesis of cofactors, prosthetic groups, and carriers, Pyridine nucleotides       | -1.21 |
| GSU2366 | rfbB   | dTDP-glucose 4,6-dehydratase                             | Biosynthesis and degradation of surface polysaccharides and lipopolysaccharides        | -1.41 |
| GSU2266 | lpxD   | UDP-3-O-3-hydroxymyristoyl glucosamine N-acyltransferase | Biosynthesis and degradation of surface polysaccharides and lipopolysaccharides        | -1.42 |
| GSU1765 |        | geranyltranstransferase                                  | Biosynthesis of cofactors, prosthetic groups, and carriers, Menaquinone and ubiquinone | -1.47 |
| GSU2004 | ubiD-2 | UbiD family decarboxylase                                | Biosynthesis of cofactors, prosthetic groups, and carriers, Menaquinone and ubiquinone | -1.57 |
| GSU2087 | gmhA   | D-sedoheptulose-7-phosphate isomerase                    | Biosynthesis and degradation of surface polysaccharides and lipopolysaccharides        | -1.63 |
| GSU0859 | galU   | UTP-glucose-1-phosphate uridylyltransferase              | Biosynthesis and degradation of surface polysaccharides and lipopolysaccharides        | -1.75 |

|         |      |  |   |       |
|---------|------|--|---|-------|
| GSU2360 |      | maltooligosyltrehalose synthase, putative    | Biosynthesis and degradation of surface polysaccharides and lipopolysaccharides | -1.76 |
| GSU0115 | pdxA | 4-hydroxythreonine-4-phosphate dehydrogenase | Biosynthesis of cofactors, prosthetic groups, and carriers, Pyridoxine          | -1.76 |
| GSU3194 | thiL | thiamine monophosphate kinase                | Biosynthesis of cofactors, prosthetic groups, and carriers, Thiamine            | -1.79 |

Table B6:  $\Delta z$ -score of proteins involved in regulatory functions.  $\Delta z$ -score was calculated as follows: (z-score in U treatment - z-score in control)

| Locus ID | Symbol | Name   | Category                                   | Dz   |
|----------|--------|--|--|------|
| GSU3292  |        | transcriptional regulator, Fur family                            | Regulatory functions, DNA interactions     | 1.79 |
| GSU0106  |        | chromosome partitioning ATPase Soj                               | Regulatory functions, Other                | 1.79 |
| GSU2980  | nikR   | nickel-binding domain transcriptional regulator                  | Regulatory functions, DNA interactions     | 1.78 |
| GSU2666  |        | transcriptional regulator, TetR family                           | Regulatory functions, DNA interactions     | 1.77 |
| GSU1117  |        | response regulator   | Regulatory functions, Protein interactions | 1.71 |
| GSU0008  |        | response receiver sensor histidine kinase, PAS domain-containing | Signal transduction, Two-component systems | 1.71 |
| GSU1999  | hfq    | hfq protein  | Regulatory functions, Other                | 1.70 |
| GSU1836  | glnB   | nitrogen regulatory protein P-II                                 | Regulatory functions,                      | 1.63 |

|         |      |   | Protein interactions                       |      |
|---------|------|---|--|------|
| GSU1270 | pyrR | pyrimidine operon regulatory protein PyrR; uracil phosphoribosyltransferase                     | Regulatory functions, Other                | 1.63 |
| GSU1415 |      | response regulator  | Signal transduction, Two-component systems | 1.61 |
| GSU3109 |      | transcriptional regulator, IclR family  | Regulatory functions, DNA interactions     | 1.60 |
| GSU3457 |      | amino acid-binding ACT domain regulatory protein  | Regulatory functions, Other                | 1.59 |
| GSU0599 |      | sensor histidine kinase   | Regulatory functions, Protein interactions | 1.59 |
| GSU2789 |      | sensor histidine kinase, PAS, PAS and PAS domain-containing                                     | Signal transduction, Two-component systems | 1.58 |
| GSU3370 |      | transcriptional regulator, GntR family  | Regulatory functions, DNA interactions     | 1.57 |
| GSU1626 |      | transcriptional regulator, GntR family  | Regulatory functions, DNA interactions     | 1.57 |
| GSU1427 |      | anti-anti-sigma factor  | Regulatory functions, Protein interactions | 1.56 |
| GSU0283 |      | sensor histidine kinase, GAF and GAF domain-containing, nonconserved putative heme-binding site | Signal transduction, Two-component systems | 1.56 |
| GSU2625 |      | transcriptional regulator, ArsR family  | Regulatory functions, DNA interactions     | 1.55 |
| GSU1039 |      | sigma-54 dependent DNA-binding response regulator   | Signal transduction, Two-component systems | 1.54 |
| GSU2698 |      | transcriptional regulator, TetR family  | Regulatory functions, DNA interactions     | 1.51 |

|         |      |  |  |      |
|---------|------|--|--|------|
| GSU2815 |      | sensory box histidine kinase                             | Signal transduction, Two-component systems | 1.48 |
| GSU0939 |      | nitrogen regulatory protein P-II, putative               | Regulatory functions, Protein interactions | 1.44 |
| GSU1414 |      | sensory box histidine kinase/response regulator          | Signal transduction, Two-component systems | 1.43 |
| GSU1379 | fur  | ferric uptake regulation protein Fur                     | Regulatory functions, DNA interactions     | 1.42 |
| GSU3253 |      | response regulator                                       | Signal transduction, Two-component systems | 1.37 |
| GSU1891 |      | response regulator                                       | Signal transduction, Two-component systems | 1.18 |
| GSU2816 |      | sensory box histidine kinase/response regulator          | Signal transduction, Two-component systems | 1.16 |
| GSU0514 |      | transcriptional regulator, IclR family                   | Regulatory functions, DNA interactions     | 1.16 |
| GSU2475 |      | sigma-54 dependent transcriptional regulator             | Regulatory functions, Protein interactions | 1.13 |
| GSU1940 |      | sigma-54 dependent DNA-binding response regulator        | Signal transduction, Two-component systems | 1.08 |
| GSU0366 |      | transcriptional regulator, putative                      | Regulatory functions, Other                | 1.08 |
| GSU3261 |      | response regulator                                       | Signal transduction, Two-component systems | 0.82 |
| GSU0682 |      | DNA-binding response regulator, LuxR family              | Regulatory functions, DNA interactions     | 0.79 |
| GSU3363 |      | sigma-54 dependent transcriptional regulator, Fis family | Regulatory functions, Protein interactions | 0.79 |
| GSU2483 | kdpD | sensor histidine kinase KdpD                             | Signal transduction, Two-component systems | 0.78 |

|         |     |   |  |      |
|---------|-----|---|--|------|
| GSU3437 |     | sensory box histidine kinase                              | Signal transduction, Two-component systems | 0.67 |
| GSU0735 |     | PTS system IIA component, fructose subfamily              | Signal transduction, PTS                   | 0.60 |
| GSU1220 |     | response regulator  | Regulatory functions, Protein interactions | 0.58 |
| GSU2354 |     | transcriptional regulator, IclR family                    | Regulatory functions, DNA interactions     | 0.50 |
| GSU2915 |     | sigma-54 dependent DNA-binding response regulator         | Regulatory functions, Protein interactions | 0.45 |
| GSU2225 |     | GTP-binding protein Era, putative                         | Regulatory functions, RNA interactions     | 0.42 |
| GSU1927 |     | sensory box/response regulator                            | Signal transduction, Two-component systems | 0.41 |
| GSU2287 |     | response regulator  | Regulatory functions, Protein interactions | 0.40 |
| GSU0881 |     | sensor histidine kinase                                   | Regulatory functions, Protein interactions | 0.34 |
| GSU3421 |     | transcriptional regulator, Crp/Fnr family                 | Regulatory functions, DNA interactions     | 0.33 |
| GSU1116 |     | GAF domain protein, putative                              | Regulatory functions, Other                | 0.32 |
| GSU0732 |     | nucleoside diphosphate kinase regulator protein, putative | Regulatory functions, Other                | 0.15 |
| GSU2226 | era | GTP-binding protein Era                                   | Regulatory functions, RNA interactions     | 0.12 |
| GSU1658 |     | response regulator/GGDEF domain protein                   | Signal transduction, Two-component systems | 0.10 |
| GSU0149 |     | sensor histidine kinase/response regulator                | Signal transduction, Two-component systems | 0.10 |

|         |      |   |   |       |
|---------|------|---|---|-------|
| GSU1129 |      | sigma-54 dependent DNA-binding response regulator | Signal transduction, Two-component systems        | 0.10  |
| GSU0811 | ntrX | nitrogen regulation protein NtrX                  | Regulatory functions, Other                       | 0.08  |
| GSU0842 |      | sensory box histidine kinase/response regulator   | Signal transduction, Two-component systems        | 0.07  |
| GSU0009 |      | sensory box histidine kinase                      | Regulatory functions, Small molecule interactions | -0.01 |
| GSU0841 |      | sigma-54 dependent DNA-binding response regulator | Signal transduction, Two-component systems        | -0.02 |
| GSU3127 |      | transcriptional regulator, AraC family            | Regulatory functions, DNA interactions            | -0.05 |
| GSU2219 |      | response regulator                                | Signal transduction, Two-component systems        | -0.18 |
| GSU1320 |      | sigma-54 dependent DNA-binding response regulator | Signal transduction, Two-component systems        | -0.21 |
| GSU2991 |      | sensor histidine kinase                           | Regulatory functions, Protein interactions        | -0.22 |
| GSU1655 |      | sensory box histidine kinase/response regulator   | Regulatory functions, Small molecule interactions | -0.25 |
| GSU1003 | ntrC | nitrogen regulation protein NR(I)                 | Regulatory functions, DNA interactions            | -0.31 |
| GSU0896 | tldD | tldD protein                                      | Regulatory functions, Other                       | -0.33 |
| GSU0303 |      | sensory box protein                               | Regulatory functions, Small molecule interactions | -0.35 |
| GSU1928 |      | sensor histidine kinase/response                  | Signal transduction, Two-                         | -0.57 |

|         |      |   |  |       |
|---------|------|---|--|-------|
|         |      | regulator   | component systems                          |       |
| GSU0963 |      | sigma-54 dependent DNA-binding response regulator | Signal transduction, Two-component systems | -0.61 |
| GSU1863 |      | transcriptional regulator, Ros/MucR family        | Regulatory functions, DNA interactions     | -0.64 |
| GSU2262 | degT | pleiotropic regulatory protein                    | Regulatory functions, Other                | -0.66 |
| GSU2523 |      | transcriptional regulator, LysR family            | Regulatory functions, DNA interactions     | -0.67 |
| GSU1119 |      | sensor histidine kinase/response regulator        | Signal transduction, Two-component systems | -0.69 |
| GSU1495 |      | sigma-54 dependent DNA-binding response regulator | Signal transduction, Two-component systems | -0.75 |
| GSU1934 |      | transcriptional activator, putative, Baf family   | Regulatory functions, DNA interactions     | -0.76 |
| GSU0776 |      | sigma-54 dependent DNA-binding response regulator | Signal transduction, Two-component systems | -0.78 |
| GSU3138 |      | sensor histidine kinase/response regulator        | Signal transduction, Two-component systems | -0.79 |
| GSU1654 |      | response regulator, putative                      | Signal transduction, Two-component systems | -0.93 |
| GSU0284 | dksA | dnaK suppressor protein                           | Regulatory functions, DNA interactions     | -0.93 |
| GSU0598 |      | sigma-54 dependent DNA-binding response regulator | Regulatory functions, DNA interactions     | -0.95 |
| GSU1579 |      | LAO/AO transport system ATPase                    | Regulatory functions, Protein interactions | -0.95 |
| GSU2947 |      | sensor histidine kinase                           | Signal transduction, Two-component systems | -0.97 |
| GSU1250 |      | sigma-54 dependent DNA-binding                    | Signal transduction, Two-                  | -0.98 |



|         |  |   |   |       |
|---------|--|---|---|-------|
|         |  | response regulator                                      | component systems                                 |       |
| GSU3087 |  | transcriptional regulator, Sir2 family                  | Regulatory functions, DNA interactions            | -1.05 |
| GSU2046 |  | response regulator                                      | Regulatory functions, Protein interactions        | -1.26 |
| GSU2016 |  | sensory box/GGDEF family protein                        | Regulatory functions, Small molecule interactions | -1.29 |
| GSU1316 |  | response regulator                                      | Signal transduction, Two-component systems        | -1.32 |
| GSU1004 |  | sensory box histidine kinase                            | Regulatory functions, Small molecule interactions | -1.35 |
| GSU1120 |  | response regulator                                      | Regulatory functions, Protein interactions        | -1.37 |
| GSU0451 |  | DNA-binding response regulator                          | Signal transduction, Two-component systems        | -1.46 |
| GSU3206 |  | zinc finger transcriptional regulator, TraR/DksA family | Regulatory functions, DNA interactions            | -1.50 |
| GSU2362 |  | transcriptional regulator, MarR family                  | Regulatory functions, DNA interactions            | -1.52 |
| GSU1941 |  | sensor histidine kinase, GAF domain-containing          | Signal transduction, Two-component systems        | -1.54 |
| GSU0452 |  | sensor histidine kinase                                 | Signal transduction, Two-component systems        | -1.56 |
| GSU1319 |  | sensor histidine kinase                                 | Regulatory functions, Protein interactions        | -1.63 |

Table B7:  $\Delta z$ -score of hypothetical proteins.  $\Delta z$ -score was calculated as follows: (z-score in U treatment - z-score in control)

| Locus ID | Name    | Category   | $\Delta z$ |
|----------|---------|--|------------|
| GSU3318  |         | conserved hypothetical protein                     | 1.80       |
| GSU0987  |         | conserved hypothetical protein                     | 1.79       |
| GSU0983  |         | phage-related baseplate assembly protein, putative | 1.78       |
| GSU2038  | pilY1-2 | type IV pilus tip-associated adhesin               | 1.78       |
| GSU0990  |         | hypothetical protein                               | 1.77       |
| GSU0672  |         | conserved hypothetical protein                     | 1.77       |
| GSU1328  |         | protein of unknown function DUF1255                | 1.76       |
| GSU2441  |         | conserved hypothetical protein                     | 1.76       |
| GSU1845  |         | conserved hypothetical protein                     | 1.69       |
| GSU2437  |         | conserved hypothetical protein                     | 1.69       |
| GSU2938  |         | conserved hypothetical protein                     | 1.69       |
| GSU3134  |         | conserved hypothetical protein                     | 1.67       |
| GSU1667  |         | conserved hypothetical protein                     | 1.67       |
| GSU3278  |         | conserved hypothetical protein                     | 1.66       |
| GSU1548  |         | hypothetical protein                               | 1.66       |
| GSU1283  |         | conserved hypothetical protein                     | 1.65       |
| GSU0478  |         | ferritin-like domain protein                       | 1.65       |
| GSU0164  |         | conserved hypothetical protein, truncation         | 1.64       |
| GSU1679  |         | hypothetical protein                               | 1.64       |
| GSU3410  |         | conserved hypothetical protein                     | 1.64       |
| GSU2906  |         | conserved hypothetical protein                     | 1.62       |
| GSU1066  | pilY1-1 | type IV pilus tip-associated adhesin               | 1.61       |
| GSU2106  |         | conserved hypothetical protein                     | 1.59       |
| GSU0384  |         | ferritin-like domain protein                       | 1.58       |
| GSU1642  |         | ferritin-like domain protein                       | 1.58       |
| GSU2742  |         | conserved hypothetical protein                     | 1.55       |
| GSU0312  |         | PilZ domain protein                                | 1.55       |

|           |  |  |      |
|-----------|--|--|------|
| GSU1376   |  | conserved hypothetical protein                                 | 1.54 |
| GSU2255   |  | glycosyl transferase, putative                                 | 1.53 |
| GSU1769   |  | divergent polysaccharide deacetylase domain protein            | 1.53 |
| GSU2426   |  | mcbC-like oxidoreductase for polypeptide thioester cyclization | 1.52 |
| GSU3306   |  | conserved hypothetical protein                                 | 1.52 |
| GSU2377   |  | conserved hypothetical protein                                 | 1.50 |
| GSU0905.1 |  | cold shock DNA/RNA-binding protein                             | 1.49 |
| GSU0141   |  | conserved hypothetical protein                                 | 1.47 |
| GSU2647   |  | nucleoside diphosphate sugar epimerase                         | 1.47 |
| GSU2332   |  | conserved hypothetical protein                                 | 1.47 |
| GSU3289   |  | ferritin-like domain protein                                   | 1.45 |
| GSU0061   |  | conserved hypothetical protein                                 | 1.44 |
| GSU0973   |  | conserved hypothetical protein                                 | 1.44 |
| GSU1565   |  | conserved hypothetical protein                                 | 1.40 |
| GSU0195   |  | protein of unknown function DUF1458                            | 1.39 |
| GSU0302   |  | conserved hypothetical protein                                 | 1.38 |
| GSU0086.1 |  | hypothetical   | 1.37 |
| GSU2713   |  | conserved hypothetical protein                                 | 1.37 |
| GSU0511   |  | leucyl aminopeptidase-related protein                          | 1.31 |
| GSU1771   |  | putative DNA/RNA-binding protein                               | 1.30 |
| GSU2564   |  | conserved hypothetical protein                                 | 1.25 |
| GSU1971   |  | hypothetical protein   | 1.25 |
| GSU2639   |  | conserved hypothetical protein                                 | 1.24 |
| GSU2710   |  | conserved hypothetical protein                                 | 1.22 |
| GSU2298   |  | conserved hypothetical protein                                 | 1.21 |
| GSU1872   |  | conserved hypothetical protein                                 | 1.19 |
| GSU2970   |  | conserved hypothetical protein                                 | 1.15 |
| GSU1969   |  | hypothetical protein   | 1.12 |

|         |   |      |
|---------|---|------|
| GSU3403 | OmpJ-related porin  | 1.10 |
| GSU2733 | conserved hypothetical protein                              | 1.09 |
| GSU2793 | conserved hypothetical protein                              | 1.04 |
| GSU0716 | conserved hypothetical protein                              | 1.02 |
| GSU1087 | conserved hypothetical protein                              | 1.00 |
| GSU3293 | ferritin-like domain protein                                | 0.92 |
| GSU0320 | conserved hypothetical protein                              | 0.91 |
| GSU2107 | hypothetical protein  | 0.89 |
| GSU1947 | hypothetical protein  | 0.89 |
| GSU2251 | hypothetical protein  | 0.87 |
| GSU2750 | conserved domain protein                                    | 0.82 |
| GSU3309 | conserved hypothetical protein                              | 0.79 |
| GSU0715 | conserved hypothetical protein                              | 0.79 |
| GSU0868 | DUF147 domain protein                                       | 0.79 |
| GSU0790 | conserved hypothetical protein                              | 0.75 |
| GSU2528 | conserved hypothetical protein                              | 0.68 |
| GSU1252 | multicopper oxidase with phosphopantotheine attachment site | 0.63 |
| GSU0874 | conserved hypothetical protein                              | 0.61 |
| GSU0005 | conserved hypothetical protein                              | 0.60 |
| GSU3185 | hypothetical protein  | 0.59 |
| GSU2276 | protein of unknown function DUF1015                         | 0.58 |
| GSU3086 | N6-adenine-specific DNA methylase, N12 class                | 0.56 |
| GSU0540 | conserved hypothetical protein                              | 0.54 |
| GSU2002 | conserved hypothetical protein                              | 0.50 |
| GSU3085 | conserved hypothetical protein                              | 0.47 |
| GSU2035 | conserved hypothetical protein                              | 0.42 |
| GSU2500 | YVTN family beta-propeller domain protein                   | 0.40 |
| GSU0481 | conserved hypothetical protein                              | 0.35 |
| GSU2440 | conserved hypothetical protein                              | 0.30 |
| GSU2048 | conserved hypothetical protein                              | 0.30 |

|          |  |   |       |
|----------|--|---|-------|
| GSU1385  |  | conserved hypothetical protein                    | 0.21  |
| GSU2108  |  | conserved hypothetical protein                    | 0.19  |
| GSU1585  |  | protein of unknown function DUF150                | 0.16  |
| GSU2644  |  | conserved hypothetical protein                    | 0.16  |
| GSU2747  |  | conserved hypothetical protein                    | 0.14  |
| GSU3351  |  | conserved hypothetical protein                    | 0.13  |
| GSU1263  |  | conserved hypothetical protein                    | 0.11  |
| GSU1876  |  | conserved hypothetical protein                    | 0.07  |
| GSU3105  |  | conserved hypothetical protein                    | 0.06  |
| GSU0165  |  | conserved hypothetical protein, truncation        | 0.04  |
| GSU3003  |  | conserved hypothetical protein                    | 0.03  |
| GSU2427  |  | conserved hypothetical protein                    | 0.03  |
| GSU1938  |  | conserved hypothetical protein                    | -0.01 |
| GSU3344  |  | conserved hypothetical protein                    | -0.02 |
| GSU0476  |  | protein of unknown function DUF185                | -0.05 |
| GSU2239  |  | YicC family stress-induced protein TIGR00255      | -0.10 |
| GSU2922  |  | conserved hypothetical protein                    | -0.10 |
| GSU2886. |  |   |       |
| 1        |  | cytochrome c, 7 heme-binding sites                | -0.20 |
| GSU0083  |  | protein of unknown function YfiH (DUF152)         | -0.21 |
| GSU3362  |  | conserved hypothetical protein                    | -0.26 |
| GSU1247  |  | conserved hypothetical protein                    | -0.27 |
| GSU3358  |  | conserved hypothetical protein                    | -0.29 |
| GSU0450  |  | protein of unknown function DUF299                | -0.34 |
| GSU1333  |  | conserved hypothetical protein                    | -0.38 |
| GSU1046  |  | conserved hypothetical protein                    | -0.39 |
| GSU1472  |  | PATAN domain protein                              | -0.40 |
| GSU2017  |  | periplasmic solute-binding protein                | -0.40 |
| GSU2105  |  | predicted ATP-dependent Lon-type protease COG4930 | -0.42 |
| GSU2682  |  | conserved hypothetical protein                    | -0.47 |

|         |       |                                    |       |
|---------|-------|------------------------------------|-------|
| GSU2200 |       | conserved hypothetical protein     | -0.49 |
| GSU2347 |       | conserved hypothetical protein     | -0.49 |
| GSU2082 |       | putative epimerase                 | -0.50 |
| GSU1181 |       | conserved hypothetical protein     | -0.50 |
| GSU0319 |       | conserved hypothetical protein     | -0.51 |
| GSU3243 |       | conserved hypothetical protein     | -0.52 |
| GSU2780 |       | conserved hypothetical protein     | -0.54 |
| GSU2086 |       | conserved hypothetical protein     | -0.57 |
| GSU0934 |       | conserved hypothetical protein     | -0.65 |
| GSU1497 |       | conserved hypothetical protein     | -0.68 |
| GSU2469 |       | hypothetical protein               | -0.70 |
| GSU0849 |       | conserved hypothetical protein     | -0.70 |
| GSU3204 |       | protein of unknown function DUF520 | -0.71 |
| GSU3301 | tmk-2 | thymidylate kinase, putative       | -0.75 |
| GSU0536 |       | ATP alpha-hydrolase TIGR00268      | -0.78 |
| GSU0564 |       | conserved hypothetical protein     | -0.79 |
| GSU1850 |       | hypothetical protein               | -0.83 |
| GSU0714 |       | hypothetical protein               | -0.83 |
| GSU2047 |       | beta-lactamase family protein      | -0.84 |
| GSU3275 |       | conserved hypothetical protein     | -0.85 |
| GSU1079 |       | hypothetical protein               | -0.92 |
| GSU1151 |       | YdjC-like protein                  | -0.98 |
| GSU1884 |       | P-loop-containing kinase           | -1.02 |
| GSU1212 |       | conserved hypothetical protein     | -1.04 |
| GSU2496 |       | conserved hypothetical protein     | -1.06 |
| GSU1829 |       | conserved hypothetical protein     | -1.07 |
| GSU0382 |       | conserved hypothetical protein     | -1.08 |
| GSU2405 |       | hypothetical protein               | -1.10 |
| GSU3244 |       | conserved hypothetical protein     | -1.13 |
| GSU1167 |       | conserved hypothetical protein     | -1.14 |

|         |      |   |       |
|---------|------|---|-------|
| GSU0882 |      | periplasmic/secreted protein DUF534                       | -1.14 |
| GSU1073 |      | conserved hypothetical protein                            | -1.15 |
| GSU3144 |      | conserved hypothetical protein                            | -1.16 |
| GSU3341 | prkA | putative serine protein kinase                            | -1.19 |
| GSU0737 |      | conserved hypothetical protein                            | -1.19 |
| GSU3305 |      | conserved hypothetical protein                            | -1.20 |
| GSU0317 |      | conserved hypothetical protein                            | -1.22 |
| GSU0081 |      | conserved hypothetical protein                            | -1.23 |
| GSU1357 |      | conserved hypothetical protein                            | -1.23 |
| GSU3337 |      | conserved hypothetical protein                            | -1.24 |
| GSU1360 |      | Sir2 superfamily protein                                  | -1.24 |
| GSU2146 |      | conserved hypothetical protein                            | -1.25 |
| GSU1282 |      | putative porin  | -1.25 |
| GSU0133 |      | conserved hypothetical protein                            | -1.26 |
| GSU2726 |      | conserved hypothetical protein                            | -1.28 |
| GSU2193 |      | ferritin-like domain protein                              | -1.28 |
| GSU0680 |      | DUF748 repeat protein                                     | -1.30 |
| GSU1889 | yhbN | conserved hypothetical protein                            | -1.30 |
| GSU3402 |      | conserved hypothetical protein                            | -1.31 |
| GSU2675 |      | C1 peptidase family protein                               | -1.32 |
| GSU0850 |      | protein disulfide bond isomerase, DsbC/DsbG-like          | -1.35 |
| GSU0095 |      | conserved hypothetical protein                            | -1.37 |
| GSU0977 |      | conserved hypothetical protein                            | -1.43 |
| GSU2518 |      | conserved hypothetical protein                            | -1.44 |
| GSU1436 |      | conserved hypothetical protein                            | -1.45 |
| GSU2359 |      | glycoside hydrolase, family 57, DUF3536 domain-containing | -1.50 |
| GSU2424 |      | conserved hypothetical protein                            | -1.52 |
| GSU2090 |      | conserved hypothetical protein                            | -1.53 |
| GSU0233 |      | protein of unknown function DUF480                        | -1.55 |
| GSU2461 |      | conserved hypothetical protein                            | -1.55 |

|         |      |  |       |
|---------|------|--|-------|
| GSU1932 |      | SPOR domain protein                            | -1.58 |
| GSU1337 |      | lipoprotein, putative                          | -1.58 |
| GSU0310 |      | phospholipase, patatin family, putative        | -1.59 |
| GSU1479 |      | conserved hypothetical protein                 | -1.60 |
| GSU2788 |      | OsmC family protein                            | -1.62 |
| GSU1000 |      | conserved hypothetical protein                 | -1.62 |
| GSU1278 |      | protein of unknown function DUF1858            | -1.63 |
| GSU2248 |      | conserved hypothetical protein                 | -1.63 |
| GSU2521 | yedF | selenium metabolism protein YedF, putative     | -1.64 |
| GSU3111 |      | conserved hypothetical protein                 | -1.64 |
| GSU0388 |      | conserved hypothetical protein                 | -1.64 |
| GSU0824 |      | conserved hypothetical protein                 | -1.64 |
| GSU2353 |      | conserved hypothetical protein                 | -1.66 |
| GSU0570 |      | SAM-dependent methyltransferase, type 11       | -1.67 |
| GSU1782 | pulM | type II secretion system ATPase PulM, putative | -1.67 |
| GSU1901 |      | conserved hypothetical protein                 | -1.69 |
| GSU0915 |      | conserved hypothetical protein                 | -1.71 |
| GSU1254 |      | hypothetical protein                           | -1.71 |
| GSU2273 |      | conserved hypothetical protein                 | -1.76 |
| GSU3139 |      | protein of unknown function DUF399             | -1.76 |
| GSU0355 |      | conserved hypothetical protein                 | -1.76 |
| GSU1060 |      | conserved hypothetical protein                 | -1.79 |
| GSU1981 |      | conserved hypothetical protein                 | -1.80 |
| GSU2998 |      | conserved hypothetical protein                 | 1.61  |

Table B8:  $\Delta z$ -score of proteins involved in transport.  $\Delta z$ -score was calculated as follows:

(z-score in U treatment - z-score in control)

| Locus ID | Symbol | Name                     | Category              | $\Delta z$ |
|----------|--------|--------------------------|-----------------------|------------|
| GSU1482  |        | efflux pump, RND family, | Transport and binding | 1.81       |



|         |      |  |   |      |
|---------|------|--|---|------|
|         |      | outer membrane protein   | proteins, Unknown substrate   |      |
| GSU0720 |      | superoxide reductase   | Transport and binding proteins, Cations and iron carrying compounds | 1.78 |
| GSU2700 | tupA | tungstate ABC transporter, periplasmic tungstate-binding protein, putative | Transport and binding proteins, Anions                              | 1.77 |
| GSU2695 |      | efflux pump, RND family, outer membrane protein                            | Transport and binding proteins, Unknown substrate                   | 1.77 |
| GSU0689 | hpnN | efflux pump, RND superfamily, putative                                     | Transport and binding proteins, Cations and iron carrying compounds | 1.75 |
| GSU1230 |      | ABC transporter, periplasmic substrate-binding protein                     | Transport and binding proteins, Unknown substrate                   | 1.72 |
| GSU0800 |      | amino acid ABC transporter, periplasmic amino acid-binding protein         | Transport and binding proteins, Amino acids, peptides and amines    | 1.71 |
| GSU2136 |      | efflux pump, RND family, membrane fusion protein                           | Transport and binding proteins, Cations and iron carrying compounds | 1.71 |
| GSU1900 |      | transporter, putative  | Transport and binding proteins, Unknown substrate                   | 1.70 |
| GSU2781 |      | efflux transporter, RND family, MFP subunit                                | Transport and binding proteins, Unknown substrate                   | 1.64 |
| GSU2008 |      | branched-chain amino acid ABC transporter, ATP-binding protein             | Transport and binding proteins, Amino acids, peptides and amines    | 1.61 |
| GSU1855 |      | polysaccharide chain length determinant domain protein                     | Transport and binding proteins, Other                               | 1.60 |
| GSU1978 | epsI | EpsI family protein  | Transport and binding   | 1.59 |

|         |        |  |   |      |
|---------|--------|--|---|------|
|         |        |  | proteins, Unknown substrate   |      |
| GSU0496 |        | efflux transporter, RND family, MFP subunit                        | Transport and binding proteins, Unknown substrate                   | 1.56 |
| GSU1678 | mgtA   | cation-transport ATPase, E1-E2 family                              | Transport and binding proteins, Cations and iron carrying compounds | 1.54 |
| GSU0212 |        | ABC transporter, ATP-binding protein                               | Transport and binding proteins, Unknown substrate                   | 1.50 |
| GSU0815 |        | ABC transporter, periplasmic substrate-binding protein, MCE family | Transport and binding proteins, Unknown substrate                   | 1.50 |
| GSU1731 | livG   | branched-chain amino acid ABC transporter, ATP-binding protein     | Transport and binding proteins, Amino acids, peptides and amines    | 1.50 |
| GSU1332 |        | heavy metal efflux pump, CzcA family                               | Transport and binding proteins, Cations and iron carrying compounds | 1.49 |
| GSU1557 |        | mechanosensitive ion channel family protein                        | Transport and binding proteins, Unknown substrate                   | 1.45 |
| GSU2260 |        | ABC transporter, ATP-binding protein, MsbA family                  | Transport and binding proteins, Other                               | 1.43 |
| GSU2351 |        | cation-transport ATPase, E1-E2 family                              | Transport and binding proteins, Cations and iron carrying compounds | 1.42 |
| GSU2452 |        | copper-translocating P-type ATPase                                 | Transport and binding proteins, Cations and iron carrying compounds | 1.38 |
| GSU3322 | corA-2 | magnesium and cobalt transport protein CorA                        | Transport and binding proteins, Cations and iron carrying compounds | 1.35 |

|         |      |   |  |      |
|---------|------|---|--|------|
| GSU1775 | ftsE | cell division ATP-binding protein FtsE  | Transport and binding proteins, Unknown substrate                          | 1.33 |
| GSU1307 | ftn  | ferritin  | Transport and binding proteins, Cations and iron carrying compounds        | 1.29 |
| GSU1481 |      | multidrug resistance protein, putative  | Transport and binding proteins, Other                                      | 1.29 |
| GSU1331 |      | efflux transporter, RND family, MFP subunit   | Transport and binding proteins, Unknown substrate                          | 1.27 |
| GSU3401 |      | branched-chain amino acid ABC transporter, periplasmic amino acid-binding protein, putative | Transport and binding proteins, Amino acids, peptides and amines           | 1.26 |
| GSU1165 | ptsP | phosphoenolpyruvate-protein phosphotransferase PtsP   | Transport and binding proteins, Carbohydrates, organic alcohols, and acids | 1.25 |
| GSU1330 |      | metal ion efflux outer membrane protein family protein, putative                            | Transport and binding proteins, Cations and iron carrying compounds        | 1.03 |
| GSU3392 |      | branched-chain amino acid ABC transporter, ATP-binding protein                              | Transport and binding proteins, Amino acids, peptides and amines           | 0.71 |
| GSU3291 |      | V-type H(+)-translocating pyrophosphatase   | Transport and binding proteins, Cations and iron carrying compounds        | 0.68 |
| GSU1883 |      | PTS system, IIA component, putative   | Transport and binding proteins, Carbohydrates, organic alcohols, and acids | 0.61 |
| GSU2055 |      | extracellular solute-binding protein, family 7  | Transport and binding proteins, Unknown substrate                          | 0.60 |
| GSU0814 |      | outer membrane efflux protein,  | Transport and binding  | 0.55 |

|         |      |   |   |       |
|---------|------|---|---|-------|
|         |      | putative  | proteins, Unknown substrate   |       |
| GSU2982 |      | TonB dependent receptor,<br>putative                                      | Transport and binding<br>proteins, Unknown substrate                      | 0.42  |
| GSU1644 |      | ABC transporter, ATP-binding<br>protein                                   | Transport and binding<br>proteins, Unknown substrate                      | 0.42  |
| GSU1501 |      | ABC transporter, ATP-binding<br>protein                                   | Transport and binding<br>proteins, Unknown substrate                      | 0.34  |
| GSU1888 |      | ABC transporter, ATP-binding<br>protein                                   | Transport and binding<br>proteins, Unknown substrate                      | 0.31  |
| GSU0025 |      | tolB protein  | Transport and binding<br>proteins, Other                                  | 0.26  |
| GSU2352 |      | sodium/solute symporter<br>family protein                                 | Transport and binding<br>proteins, Unknown substrate                      | 0.12  |
| GSU2951 |      | ABC transporter, ATP-binding<br>protein                                   | Transport and binding<br>proteins, Unknown substrate                      | -0.02 |
| GSU0940 |      | ammonium transporter  | Transport and binding<br>proteins, Cations and iron<br>carrying compounds | -0.03 |
| GSU0391 |      | Outer membrane efflux family<br>protein                                   | Transport and binding<br>proteins, Unknown substrate                      | -0.04 |
| GSU2649 |      | amino acid ABC transporter,<br>amino acid-binding protein                 | Transport and binding<br>proteins, Amino acids,<br>peptides and amines    | -0.04 |
| GSU2985 |      | ABC transporter, ATP-binding<br>protein                                   | Transport and binding<br>proteins, Unknown substrate                      | -0.16 |
| GSU3406 |      | amino acid ABC transporter,<br>periplasmic amino acid-<br>binding protein | Transport and binding<br>proteins, Amino acids,<br>peptides and amines    | -0.19 |
| GSU1730 | livF | branched-chain amino acid<br>ABC transporter, ATP-binding                 | Transport and binding<br>proteins, Amino acids,                           | -0.21 |

|         |      |  |  |       |
|---------|------|--|--|-------|
|         |      | protein  | peptides and amines  |       |
| GSU1341 |      | ABC transporter, ATP-binding protein                           | Transport and binding proteins, Unknown substrate                          | -0.21 |
| GSU1162 |      | ABC transporter, ATP-binding protein                           | Transport and binding proteins, Unknown substrate                          | -0.21 |
| GSU3391 |      | branched-chain amino acid ABC transporter, ATP-binding protein | Transport and binding proteins, Amino acids, peptides and amines           | -0.22 |
| GSU1346 | cysP | sulfate ABC transporter, periplasmic sulfate-binding protein   | Transport and binding proteins, Anions                                     | -0.23 |
| GSU0210 |      | ABC transporter, permease protein, putative                    | Transport and binding proteins, Unknown substrate                          | -0.30 |
| GSU1068 |      | sodium/solute symporter family protein                         | Transport and binding proteins, Unknown substrate                          | -0.36 |
| GSU2696 |      | AcrB/AcrD/AcrF family protein                                  | Transport and binding proteins, Other                                      | -0.38 |
| GSU1261 |      | ABC transporter, ATP-binding protein                           | Transport and binding proteins, Unknown substrate                          | -0.42 |
| GSU1016 |      | potassium uptake protein, Trk family                           | Transport and binding proteins, Cations and iron carrying compounds        | -0.45 |
| GSU1349 | cysA | sulfate ABC transporter, ATP-binding protein                   | Transport and binding proteins, Anions                                     | -0.57 |
| GSU1445 |      | TonB-dependent receptor, putative                              | Transport and binding proteins, Cations and iron carrying compounds        | -0.60 |
| GSU2751 | dcuB | C4-dicarboxylate transporter, anaerobic                        | Transport and binding proteins, Carbohydrates, organic alcohols, and acids | -0.76 |

|         |      |   |  |       |
|---------|------|---|--|-------|
| GSU3304 |      | LamB porin family protein, putative   | Transport and binding proteins, Porins                                     | -0.81 |
| GSU0028 | tolQ | tolQ protein  | Transport and binding proteins, Other                                      | -0.88 |
| GSU2782 |      | AcrB/AcrD/AcrF family protein   | Transport and binding proteins, Other                                      | -0.91 |
| GSU1735 |      | branched-chain amino acid ABC transporter, periplasmic amino acid-binding protein, putative | Transport and binding proteins, Amino acids, peptides and amines           | -0.98 |
| GSU3404 |      | amino acid ABC transporter, ATP-binding protein   | Transport and binding proteins, Amino acids, peptides and amines           | -1.01 |
| GSU2651 |      | amino acid ABC transporter, ATP-binding protein   | Transport and binding proteins, Amino acids, peptides and amines           | -1.02 |
| GSU1885 | hprK | HPr(Ser) kinase/phosphatase   | Transport and binding proteins, Carbohydrates, organic alcohols, and acids | -1.12 |
| GSU1734 |      | branched-chain amino acid ABC transporter, periplasmic amino acid-binding protein, putative | Transport and binding proteins, Amino acids, peptides and amines           | -1.13 |
| GSU0392 |      | efflux transporter, RND family, MFP subunit   | Transport and binding proteins, Unknown substrate                          | -1.14 |
| GSU0883 |      | ferric enterobactin receptor, putative  | Transport and binding proteins, Cations and iron carrying compounds        | -1.16 |
| GSU2005 |      | branched-chain amino acid ABC transporter, periplasmic amino acid-binding protein,          | Transport and binding proteins, Amino acids, peptides and amines           | -1.16 |

|         |      |   |   |       |
|---------|------|---|---|-------|
|         |      | putative  |   |       |
| GSU1161 |      | efflux transporter, RND family, MFP subunit                   | Transport and binding proteins, Unknown substrate                   | -1.20 |
| GSU0922 |      | ABC transporter, ATP-binding protein                          | Transport and binding proteins, Unknown substrate                   | -1.24 |
| GSU1340 |      | ABC transporter, permease protein                             | Transport and binding proteins, Unknown substrate                   | -1.28 |
| GSU1070 |      | sodium/solute symporter family protein                        | Transport and binding proteins, Unknown substrate                   | -1.32 |
| GSU1578 |      | B12-binding protein   | Transport and binding proteins, Other                               | -1.45 |
| GSU0813 |      | organic solvent tolerance ABC transporter periplasmic protein | Transport and binding proteins, Unknown substrate                   | -1.49 |
| GSU2697 | acrA | efflux pump, RND family, membrane fusion lipoprotein          | Transport and binding proteins, Other                               | -1.52 |
| GSU0913 | uup  | DNA-binding ATPase Uup  | Transport and binding proteins, Unknown substrate                   | -1.57 |
| GSU2665 |      | efflux pump, RND family, membrane fusion lipoprotein          | Transport and binding proteins, Unknown substrate                   | -1.57 |
| GSU0169 |      | ABC transporter, ATP-binding protein                          | Transport and binding proteins, Unknown substrate                   | -1.58 |
| GSU2413 |      | ABC transporter, ATP-binding protein                          | Transport and binding proteins, Unknown substrate                   | -1.60 |
| GSU0027 |      | ExbD/TolR-related biopolymer transport membrane protein       | Transport and binding proteins, Cations and iron carrying compounds | -1.60 |
| GSU3405 |      | amino acid ABC transporter, permease protein                  | Transport and binding proteins, Amino acids, peptides and amines    | -1.63 |
| GSU2270 | lolE | lipoprotein release ABC                                       | Transport and binding   | -1.71 |

|         |  |  |   |       |
|---------|--|--|---|-------|
|         |  | transporter, membrane protein                                  | proteins, Unknown substrate                       |       |
| GSU0949 |  | efflux transporter, RND family, MFP subunit                    | Transport and binding proteins, Unknown substrate | -1.72 |
| GSU2939 |  | porin, putative  | Transport and binding proteins, Porins            | -1.74 |
| GSU1609 |  | efflux pump, RND family, outer membrane protein                | Transport and binding proteins, Unknown substrate | -1.76 |
| GSU0816 |  | organic solvent tolerance ABC transporter, ATP-binding protein | Transport and binding proteins, Unknown substrate | -1.76 |
| GSU2187 |  | ABC transporter, permease protein                              | Transport and binding proteins, Unknown substrate | -1.81 |

Table B9:  $\Delta z$ -score of proteins involved in energy metabolism.  $\Delta z$ -score was calculated as follows: (z-score in U treatment - z-score in control)

| Locus ID | Symbol | Name   | Category                              | $\Delta z$ |
|----------|--------|--|---------------------------------------|------------|
| GSU1737  | paaK-2 | phenylacetate-CoA ligase   | Energy metabolism, Other              | 1.81       |
| GSU3246  | prx-2  | peroxiredoxin, typical 2-Cys subfamily                           | Energy metabolism, Electron transport | 1.80       |
| GSU1155  |        | glutaredoxin family protein                                      | Energy metabolism, Electron transport | 1.77       |
| GSU0357  |        | cytochrome c family protein                                      | Energy metabolism, Electron transport | 1.74       |
| GSU3296  | glcD-1 | D-lactate/glycolate dehydrogenase, FAD-binding protein, putative | Energy metabolism, Other              | 1.74       |
| GSU1648  | macC   | cytochrome c, 5 heme-binding sites                               | Energy metabolism, Electron transport | 1.73       |
| GSU2801  |        | cytochrome c, 5 heme-binding                                     | Energy metabolism, Electron           | 1.72       |



|         |        |   |  |      |
|---------|--------|---|--|------|
|         |        | sites   | transport  |      |
| GSU1089 |        | iron-sulfur cluster-binding protein                               | Energy metabolism, Electron transport                              | 1.72 |
| GSU0783 |        | nickel-dependent hydrogenase, iron-sulfur cluster-binding protein | Energy metabolism, Electron transport                              | 1.71 |
| GSU1729 |        | phenylacetate-CoA ligase  | Energy metabolism, Other   | 1.70 |
| GSU2814 |        | rubrerythrin  | Energy metabolism, Electron transport                              | 1.69 |
| GSU1606 | rpiB   | ribose-5-phosphate isomerase B, putative                          | Energy metabolism, Pentose phosphate pathway                       | 1.68 |
| GSU3423 | tkt    | transketolase   | Energy metabolism, Pentose phosphate pathway                       | 1.68 |
| GSU0601 |        | glycoside hydrolase, putative                                     | Energy metabolism, Biosynthesis and degradation of polysaccharides | 1.67 |
| GSU2101 |        | glycerol dehydratase, putative                                    | Energy metabolism, Fermentation                                    | 1.63 |
| GSU0345 | nuoH-1 | NADH dehydrogenase I, H subunit                                   | Energy metabolism, Electron transport                              | 1.62 |
| GSU2761 |        | FAD-dependent glycerol-3-phosphate dehydrogenase subunit          | Energy metabolism, Other   | 1.61 |
| GSU2286 | eno    | enolase   | Energy metabolism, Glycolysis/gluconeogenesis                      | 1.60 |
| GSU2718 | hoxL   | bidirectional NAD-reducing hydrogenase, large subunit             | Energy metabolism, Electron transport                              | 1.60 |
| GSU2013 |        | phosphoglucomutase/phosphomannomutase family protein              | Energy metabolism, Sugars  | 1.59 |
| GSU3395 | putA   | proline dehydrogenase/delta-1-                                    | Energy metabolism, Amino   | 1.58 |

|         |       |  |   |      |
|---------|-------|--|---|------|
|         |       | pyrroline-5-carboxylate dehydrogenase                                    | acids and amines                          |      |
| GSU1467 | korD  | 2-oxoglutarate:ferredoxin oxidoreductase, ferredoxin subunit             | Energy metabolism, Electron transport     | 1.55 |
| GSU1108 |       | aldehyde dehydrogenase family protein                                    | Energy metabolism, Fermentation           | 1.55 |
| GSU0728 | ppk-2 | polyphosphate kinase   | Energy metabolism, Other                  | 1.55 |
| GSU2796 | etfA  | electron transfer flavoprotein, alpha subunit                            | Energy metabolism, Electron transport     | 1.50 |
| GSU1860 | vorB  | 2-oxoacid:ferredoxin oxidoreductase, thiamin diphosphate-binding subunit | Energy metabolism, Fermentation           | 1.50 |
| GSU0088 |       | heterodisulfide reductase subunit  | Energy metabolism, Electron transport     | 1.48 |
| GSU2192 | cbbZ  | phosphoglycolate phosphatase   | Energy metabolism, Sugars                 | 1.48 |
| GSU2052 |       | indolepyruvate ferredoxin oxidoreductase, beta subunit, putative         | Energy metabolism, Fermentation           | 1.47 |
| GSU2240 | galE  | UDP-glucose 4-epimerase  | Energy metabolism, Sugars                 | 1.47 |
| GSU1707 |       | group II decarboxylase   | Energy metabolism, Amino acids and amines | 1.44 |
| GSU0804 | WrbA  | trp repressor binding protein WrbA                                       | Energy metabolism, Electron transport     | 1.44 |
| GSU3238 |       | Rieske 2Fe-2S family protein   | Energy metabolism, Electron transport     | 1.43 |
| GSU0089 |       | heterodisulfide reductase subunit  | Energy metabolism, Electron transport     | 1.43 |
| GSU2201 |       | cytochrome c family protein  | Energy metabolism, Electron transport     | 1.42 |

|         |      |   |  |      |
|---------|------|---|--|------|
| GSU1859 |      | keto/oxoacid ferredoxin oxidoreductase, gamma subunit             | Energy metabolism, Fermentation              | 1.41 |
| GSU2811 | hsc  | cytochrome c Hsc  | Energy metabolism, Electron transport        | 1.38 |
| GSU2645 |      | cytochrome c family protein                                       | Energy metabolism, Electron transport        | 1.37 |
| GSU0375 | gcvT | glycine cleavage system T protein                                 | Energy metabolism, Amino acids and amines    | 1.34 |
| GSU3294 |      | rubredoxin-oxygen oxidoreductase, putative                        | Energy metabolism, Electron transport        | 1.30 |
| GSU3302 |      | methylmalonyl-CoA mutase, putative                                | Energy metabolism, Fermentation              | 1.30 |
| GSU0385 |      | NADH dehydrogenase subunit, putative                              | Energy metabolism, Electron transport        | 1.29 |
| GSU0122 |      | nickel-dependent hydrogenase, large subunit                       | Energy metabolism, Electron transport        | 1.27 |
| GSU3374 | rpe  | ribulose-phosphate 3-epimerase                                    | Energy metabolism, Pentose phosphate pathway | 1.25 |
| GSU1334 |      | cytochrome c family protein                                       | Energy metabolism, Electron transport        | 1.25 |
| GSU1305 |      | Glu/Leu/Phe/Val dehydrogenase family protein                      | Energy metabolism, Amino acids and amines    | 1.25 |
| GSU2053 |      | indolepyruvate ferredoxin oxidoreductase, alpha subunit, putative | Energy metabolism, Fermentation              | 1.24 |
| GSU3321 |      | phosphoglucomutase/phosphomannomutase family protein              | Energy metabolism, Sugars                    | 1.24 |
| GSU2732 |      | cytochrome c family protein                                       | Energy metabolism, Electron transport        | 1.23 |

|         |        |   |   |      |
|---------|--------|---|---|------|
| GSU2706 |        | phosphate acetyltransferase                             | Energy metabolism, Electron transport         | 1.22 |
| GSU1372 |        | 3-hydroxyisobutyrate dehydrogenase family protein       | Energy metabolism, Amino acids and amines     | 1.21 |
| GSU1416 |        | iron-sulfur cluster-binding protein                     | Energy metabolism, Electron transport         | 1.12 |
| GSU0340 | nuoC   | NADH dehydrogenase I, C subunit                         | Energy metabolism, Electron transport         | 1.02 |
| GSU0843 |        | NADH oxidase, putative                                  | Energy metabolism, Electron transport         | 1.00 |
| GSU1612 | gpm    | phosphoglycerate mutase                                 | Energy metabolism, Glycolysis/gluconeogenesis | 1.00 |
| GSU1739 |        | indolepyruvate ferredoxin oxidoreductase, alpha subunit | Energy metabolism, Fermentation               | 0.98 |
| GSU3334 |        | cytochrome c family protein, putative                   | Energy metabolism, Electron transport         | 0.98 |
| GSU0339 | nuoB   | NADH dehydrogenase I, B subunit                         | Energy metabolism, Electron transport         | 0.97 |
| GSU3254 |        | phosphoglucomutase/phosphomannomutase family protein    | Energy metabolism, Sugars                     | 0.96 |
| GSU1703 | pfk    | 6-phosphofructokinase                                   | Energy metabolism, Glycolysis/gluconeogenesis | 0.95 |
| GSU2292 | ald    | alanine dehydrogenase                                   | Energy metabolism, Amino acids and amines     | 0.94 |
| GSU0350 | nuoM-1 | NADH dehydrogenase I, M subunit                         | Energy metabolism, Electron transport         | 0.88 |
| GSU3281 | trx    | thioredoxin   | Energy metabolism, Electron transport         | 0.77 |
| GSU0109 | atpF   | ATP synthase F0, B subunit                              | Energy metabolism, ATP-proton motive force    | 0.74 |

|         |        |   |  |      |
|---------|--------|---|--|------|
|         |        |   | interconversion  |      |
| GSU2449 | sucA   | 2-oxoglutarate dehydrogenase, E1 component        | Energy metabolism, TCA cycle                                       | 0.73 |
| GSU2428 | pyc    | pyruvate carboxylase                              | Energy metabolism, Glycolysis/gluconeogenesis                      | 0.73 |
| GSU1058 | sucC   | succinyl-CoA synthase, beta subunit               | Energy metabolism, TCA cycle                                       | 0.68 |
| GSU1113 |        | carbohydrate kinase, PfkB family                  | Energy metabolism, Sugars  | 0.68 |
| GSU2707 | ackA-1 | acetate kinase                                    | Energy metabolism, Fermentation                                    | 0.60 |
| GSU2068 |        | 6-phosphofructokinase                             | Energy metabolism, Glycolysis/gluconeogenesis                      | 0.48 |
| GSU2724 |        | cytochrome c family protein                       | Energy metabolism, Electron transport                              | 0.46 |
| GSU1628 |        | phosphoglycerate kinase/triosephosphate isomerase | Energy metabolism, Glycolysis/gluconeogenesis                      | 0.44 |
| GSU1996 |        | cytochrome c family protein                       | Energy metabolism, Electron transport                              | 0.42 |
| GSU2098 | cooS   | carbon monoxide dehydrogenase subunit             | Energy metabolism, Other   | 0.39 |
| GSU1284 |        | cytochrome c, putative                            | Energy metabolism, Electron transport                              | 0.35 |
| GSU0090 |        | heterodisulfide reductase subunit                 | Energy metabolism, Electron transport                              | 0.32 |
| GSU2636 |        | alpha-amylase family protein                      | Energy metabolism, Biosynthesis and degradation of polysaccharides | 0.30 |
| GSU0371 |        | carbohydrate phosphorylase                        | Energy metabolism,   | 0.29 |

|         |        |  |   |      |
|---------|--------|--|---|------|
|         |        | family protein   | Biosynthesis and degradation of polysaccharides |      |
| GSU0580 | ppdK   | pyruvate phosphate dikinase  | Energy metabolism, Other                        | 0.23 |
| GSU3385 | pckA   | phosphoenolpyruvate carboxykinase  | Energy metabolism, Glycolysis/gluconeogenesis   | 0.23 |
| GSU1564 |        | Glu/Leu/Phe/Val dehydrogenase family protein                                 | Energy metabolism, Amino acids and amines       | 0.18 |
| GSU3303 |        | methylmalonyl-CoA epimerase  | Energy metabolism, Fermentation                 | 0.17 |
| GSU0594 |        | cytochrome c family protein  | Energy metabolism, Electron transport           | 0.14 |
| GSU2588 | lpdA-2 | alpha keto acid dehydrogenase complex, E3 component, lipoamide dehydrogenase | Energy metabolism, Amino acids and amines       | 0.13 |
| GSU2308 | scfA   | malate oxidoreductase  | Energy metabolism, Other                        | 0.13 |
| GSU1660 | acnB   | aconitate hydratase 2  | Energy metabolism, TCA cycle                    | 0.11 |
| GSU3408 |        | L-threonine aldolase, low-specificity  | Energy metabolism, Amino acids and amines       | 0.09 |
| GSU2445 |        | aconitate hydratase, putative  | Energy metabolism, TCA cycle                    | 0.09 |
| GSU0466 | macA   | cytochrome c551 peroxidase   | Energy metabolism, Electron transport           | 0.08 |
| GSU1059 | sucD   | succinyl-CoA synthase, alpha subunit   | Energy metabolism, TCA cycle                    | 0.07 |
| GSU0344 |        | NADH dehydrogenase I, G subunit, putative                                    | Energy metabolism, Electron transport           | 0.06 |
| GSU0378 |        | glycine cleavage system P protein, subunit 2                                 | Energy metabolism, Amino acids and amines       | 0.06 |
| GSU0343 | nouF   | NADH dehydrogenase I, F  | Energy metabolism, Electron                     | 0.05 |

|         |        |  |   |       |
|---------|--------|--|---|-------|
|         |        | subunit  | transport                                       |       |
| GSU0785 |        | nickel-dependent hydrogenase,<br>large subunit                         | Energy metabolism, Electron<br>transport        | 0.02  |
| GSU2918 |        | transketolase, C-terminal<br>subunit                                   | Energy metabolism, Pentose<br>phosphate pathway | 0.01  |
| GSU0893 |        | thioredoxin peroxidase   | Energy metabolism, Electron<br>transport        | 0.00  |
| GSU0097 |        | pyruvate ferredoxin/ flavodoxin<br>oxidoreductase                      | Energy metabolism,<br>Fermentation              | 0.00  |
| GSU2937 |        | cytochrome c family protein  | Energy metabolism, Electron<br>transport        | -0.06 |
| GSU2872 |        | electron transfer flavoprotein,<br>Etf beta-subunit/FixA family        | Energy metabolism, Electron<br>transport        | -0.06 |
| GSU0201 | iorB   | isoquinoline 1-oxidoreductase,<br>beta subunit                         | Energy metabolism,<br>Fermentation              | -0.08 |
| GSU0777 | fdnG   | formate dehydrogenase, major<br>subunit, selenocysteine-<br>containing | Energy metabolism, Anaerobic                    | -0.08 |
| GSU1893 |        | carbohydrate isomerase,<br>KpsF/GutQ family                            | Energy metabolism, Sugars                       | -0.10 |
| GSU0742 |        | NAD-dependent<br>dehydrogenase subunit                                 | Energy metabolism, Electron<br>transport        | -0.17 |
| GSU0346 | nuoI-1 | NADH dehydrogenase I, I<br>subunit                                     | Energy metabolism, Electron<br>transport        | -0.20 |
| GSU0364 | cyd-1  | cytochrome c3  | Energy metabolism, Electron<br>transport        | -0.22 |
| GSU2898 |        | high-molecular-weight<br>cytochrome c                                  | Energy metabolism, Electron<br>transport        | -0.34 |
| GSU1761 |        | cytochrome c family protein  | Energy metabolism, Electron<br>transport        | -0.35 |

|         |         |  |  |       |
|---------|---------|--|--|-------|
| GSU3259 |         | cytochrome c family protein                        | Energy metabolism, Electron transport                      | -0.36 |
| GSU0349 | nuoL-1  | NADH dehydrogenase I, L subunit                    | Energy metabolism, Electron transport                      | -0.37 |
| GSU2504 | OmcS    | cytochrome c family protein                        | Energy metabolism, Electron transport                      | -0.39 |
| GSU0818 |         | aldehyde dehydrogenase family protein              | Energy metabolism, Fermentation                            | -0.41 |
| GSU0347 | nouJ    | NADH dehydrogenase I, J subunit                    | Energy metabolism, Electron transport                      | -0.43 |
| GSU1176 |         | fumarate reductase, cytochrome b subunit, putative | Energy metabolism, Anaerobic                               | -0.45 |
| GSU0091 |         | heterodisulfide reductase subunit                  | Energy metabolism, Electron transport                      | -0.46 |
| GSU0743 |         | NAD-dependent dehydrogenase subunit                | Energy metabolism, Electron transport                      | -0.48 |
| GSU0592 |         | cytochrome c family protein                        | Energy metabolism, Electron transport                      | -0.50 |
| GSU1465 | icd     | isocitrate dehydrogenase, NADP-dependent           | Energy metabolism, TCA cycle                               | -0.50 |
| GSU0846 | acnA    | aconitate hydratase 1                              | Energy metabolism, TCA cycle                               | -0.54 |
| GSU3444 | nuoBC D | NADH dehydrogenase I, B/C/D subunits               | Energy metabolism, Electron transport                      | -0.56 |
| GSU2887 |         | cytochrome c family protein                        | Energy metabolism, Electron transport                      | -0.57 |
| GSU0112 | atpG    | ATP synthase F1, gamma subunit                     | Energy metabolism, ATP-proton motive force interconversion | -0.58 |
| GSU1451 |         | 3-hydroxyisobutyrate                               | Energy metabolism, Amino                                   | -0.60 |



|         |        |  |  |       |
|---------|--------|--|--|-------|
|         |        | dehydrogenase family protein   | acids and amines   |       |
| GSU3125 |        | alcohol dehydrogenase, zinc-containing   | Energy metabolism, Fermentation                                    | -0.61 |
| GSU1023 | glgA-1 | glycogen synthase  | Energy metabolism, Biosynthesis and degradation of polysaccharides | -0.62 |
| GSU2762 | glpK   | glycerol kinase  | Energy metabolism, Other   | -0.71 |
| GSU2448 | sucB   | 2-oxoglutarate dehydrogenase, E2 component, dihydrolipoamide succinyltransferase | Energy metabolism, TCA cycle                                       | -0.72 |
| GSU2076 |        | cytochrome c family protein  | Energy metabolism, Electron transport                              | -0.73 |
| GSU2944 |        | (R)-2-hydroxyglutaryl-CoA dehydratase alpha-subunit, putative                    | Energy metabolism, Amino acids and amines                          | -0.74 |
| GSU0333 | atpE   | ATP synthase F0, C subunit   | Energy metabolism, ATP-proton motive force interconversion         | -0.75 |
| GSU0674 | hcP-1  | prismane protein   | Energy metabolism, Electron transport                              | -0.75 |
| GSU2797 | etfB   | electron transfer flavoprotein, beta subunit                                     | Energy metabolism, Electron transport                              | -0.77 |
| GSU0509 | sfrA   | Fe(III) reductase, alpha subunit   | Energy metabolism, Anaerobic                                       | -0.81 |
| GSU2731 | OmcC   | polyheme membrane-associated cytochrome c  | Energy metabolism, Anaerobic                                       | -0.84 |
| GSU0110 | atpH   | ATP synthase F1, delta subunit   | Energy metabolism, ATP-proton motive force interconversion         | -0.88 |
| GSU3137 |        | cytochrome c family protein  | Energy metabolism, Electron  | -0.90 |

|         |        |   |   |       |
|---------|--------|---|---|-------|
|         |        |   | transport   |       |
| GSU3256 | galT   | galactose-1-phosphate<br>uridylyltransferase                                      | Energy metabolism, Sugars   | -0.94 |
| GSU2612 |        | rubrerythrin/rubredoxin<br>protein, putative                                      | Energy metabolism, Electron<br>transport                          | -0.94 |
| GSU1470 |        | keto/oxoacid ferredoxin<br>oxidoreductase, gamma<br>subunit                       | Energy metabolism,<br>Fermentation                                | -0.95 |
| GSU2725 |        | cytochrome c family protein   | Energy metabolism, Electron<br>transport                          | -1.01 |
| GSU2446 | lpdA-1 | 2-oxoglutarate dehydrogenase<br>complex, E3 component,<br>lipoamide dehydrogenase | Energy metabolism, TCA<br>cycle                                   | -1.01 |
| GSU2919 |        | transketolase, N-terminal<br>subunit  | Energy metabolism, Pentose<br>phosphate pathway                   | -1.02 |
| GSU3331 | pyk    | pyruvate kinase   | Energy metabolism,<br>Glycolysis/gluconeogenesis                  | -1.03 |
| GSU1738 |        | indolepyruvate ferredoxin<br>oxidoreductase, beta subunit                         | Energy metabolism,<br>Fermentation                                | -1.04 |
| GSU1245 |        | fructose-bisphosphate aldolase,<br>class-II, putative                             | Energy metabolism,<br>Glycolysis/gluconeogenesis                  | -1.05 |
| GSU2495 |        | cytochrome c family protein   | Energy metabolism, Electron<br>transport                          | -1.05 |
| GSU2503 | OmcT   | cytochrome c family protein   | Energy metabolism, Electron<br>transport                          | -1.05 |
| GSU0114 | atpC   | ATP synthase F1, epsilon<br>subunit   | Energy metabolism, ATP-<br>proton motive force<br>interconversion | -1.06 |
| GSU2361 |        | alpha amylase family protein  | Energy metabolism,<br>Biosynthesis and degradation                | -1.06 |

|         |        |  |  |       |
|---------|--------|--|--|-------|
|         |        |  | of polysaccharides   |       |
| GSU0341 | nouD   | NADH dehydrogenase I, D subunit                                  | Energy metabolism, Electron transport                              | -1.06 |
| GSU2066 | glgP   | glycogen phosphorylase   | Energy metabolism, Biosynthesis and degradation of polysaccharides | -1.07 |
| GSU0274 |        | cytochrome c family protein                                      | Energy metabolism, Electron transport                              | -1.09 |
| GSU0612 | ppcA   | cytochrome c3  | Energy metabolism, Electron transport                              | -1.16 |
| GSU0342 | nuoE-1 | NADH dehydrogenase I, E subunit                                  | Energy metabolism, Electron transport                              | -1.17 |
| GSU1700 | maeB   | NADP-dependent malic enzyme                                      | Energy metabolism, TCA cycle                                       | -1.18 |
| GSU0510 | sfrB   | Fe(III) reductase, beta subunit                                  | Energy metabolism, Anaerobic                                       | -1.19 |
| GSU1377 |        | 3-hydroxybutyryl-CoA dehydratase                                 | Energy metabolism, Fermentation                                    | -1.20 |
| GSU0087 |        | heterodisulfide reductase, iron-sulfur binding subunit, putative | Energy metabolism, Electron transport                              | -1.21 |
| GSU0994 | fumB   | fumarate hydratase, class I                                      | Energy metabolism, TCA cycle                                       | -1.21 |
| GSU0479 | aspA   | aspartate ammonia-lyase  | Energy metabolism, Amino acids and amines                          | -1.21 |
| GSU0006 | gpsA   | glycerol-3-phosphate dehydrogenase (NAD(P)+)                     | Energy metabolism, Other   | -1.26 |
| GSU0591 |        | cytochrome c family protein                                      | Energy metabolism, Electron transport                              | -1.28 |
| GSU1466 | mdh    | malate dehydrogenase   | Energy metabolism, TCA cycle                                       | -1.28 |
| GSU1178 | frdB   | fumarate reductase, iron-sulfur                                  | Energy metabolism, Anaerobic                                       | -1.30 |

|         |       |  |  |       |
|---------|-------|--|--|-------|
|         |       | protein                                      |  |       |
| GSU0092 |       | heterodisulfide reductase subunit            | Energy metabolism, Electron transport                              | -1.31 |
| GSU2513 |       | cytochrome c family protein                  | Energy metabolism, Electron transport                              | -1.33 |
| GSU0377 |       | glycine cleavage system P protein, subunit 1 | Energy metabolism, Amino acids and amines                          | -1.35 |
| GSU0778 | fdnH  | formate dehydrogenase, iron-sulfur subunit   | Energy metabolism, Anaerobic                                       | -1.37 |
| GSU1397 |       | cytochrome c family protein, putative        | Energy metabolism, Electron transport                              | -1.38 |
| GSU1024 | cyd-4 | cytochrome c3                                | Energy metabolism, Electron transport                              | -1.38 |
| GSU1629 | gap   | glyceraldehyde 3-phosphate dehydrogenase 1   | Energy metabolism, Glycolysis/gluconeogenesis                      | -1.39 |
| GSU2795 |       | iron-sulfur cluster-binding protein          | Energy metabolism, Electron transport                              | -1.40 |
| GSU1182 | malQ  | 4-alpha-glucanotransferase                   | Energy metabolism, Biosynthesis and degradation of polysaccharides | -1.41 |
| GSU1177 | frdA  | fumarate reductase, flavoprotein subunit     | Energy metabolism, TCA cycle                                       | -1.42 |
| GSU2637 |       | alcohol dehydrogenase, zinc-containing       | Energy metabolism, Fermentation                                    | -1.43 |
| GSU1651 | fbP-1 | fructose-1,6-bisphosphatase                  | Energy metabolism, Glycolysis/gluconeogenesis                      | -1.44 |
| GSU0113 | atpD  | ATP synthase F1, beta subunit                | Energy metabolism, ATP-proton motive force interconversion         | -1.49 |
| GSU3207 | gpmI  | phosphoglycerate mutase, 2,3-                | Energy metabolism,   | -1.50 |

|         |       |   |  |       |
|---------|-------|---|--|-------|
|         |       | bisphosphoglycerate-independent   | Glycolysis/gluconeogenesis                                 |       |
| GSU0782 | hybS  | periplasmically oriented, membrane-bound [NiFe]-hydrogenase small subunit     | Energy metabolism, Electron transport                      | -1.54 |
| GSU0108 |       | ATP synthase F0, B subunit  | Energy metabolism, ATP-proton motive force interconversion | -1.59 |
| GSU1469 | korB  | 2-oxoglutarate:ferredoxin oxidoreductase, thiamin diphosphate-binding subunit | Energy metabolism, Fermentation                            | -1.59 |
| GSU1861 | vorA  | 2-oxoacid:ferredoxin oxidoreductase, alpha subunit                            | Energy metabolism, Fermentation                            | -1.59 |
| GSU0771 |       | zinc-dependent oxidoreductase   | Energy metabolism, Fermentation                            | -1.61 |
| GSU0803 | ppsA  | phosphoenolpyruvate synthase  | Energy metabolism, Glycolysis/gluconeogenesis              | -1.62 |
| GSU2957 | trx-2 | thioredoxin family protein  | Energy metabolism, Electron transport                      | -1.65 |
| GSU1106 | gltA  | citrate synthase  | Energy metabolism, TCA cycle                               | -1.66 |
| GSU2743 |       | cytochrome c, 1 heme-binding site   | Energy metabolism, Electron transport                      | -1.66 |
| GSU1311 | pgi   | glucose-6-phosphate isomerase   | Energy metabolism, Glycolysis/gluconeogenesis              | -1.67 |
| GSU1468 | korA  | 2-oxoglutarate:ferredoxin oxidoreductase, alpha subunit                       | Energy metabolism, Fermentation                            | -1.68 |
| GSU2737 | OmcB  | polyheme membrane-associated cytochrome c                                     | Energy metabolism, Anaerobic                               | -1.69 |
| GSU1975 |       | NAD-dependent   | Energy metabolism, Sugars                                  | -1.69 |

|         |        |   |  |       |
|---------|--------|---|--|-------|
|         |        | epimerase/dehydratase family protein                        |  |       |
| GSU0111 | atpA   | ATP synthase F1, alpha subunit                              | Energy metabolism, ATP-proton motive force interconversion | -1.74 |
| GSU1754 | kamA   | L-lysine 2,3-aminomutase                                    | Energy metabolism, Amino acids and amines                  | -1.74 |
| GSU2813 | ccpA   | cytochrome c peroxidase, 2 heme-binding sites               | Energy metabolism, Electron transport                      | -1.75 |
| GSU1321 | trx-1  | TlpA family-related protein disulfide reductase lipoprotein | Energy metabolism, Electron transport                      | -1.76 |
| GSU0488 | trxB   | thioredoxin reductase                                       | Energy metabolism, Electron transport                      | -1.78 |
| GSU0376 | gcvH-1 | glycine cleavage system H protein                           | Energy metabolism, Amino acids and amines                  | -1.78 |

Table B10:  $\Delta z$ -score of proteins involved in cellular processes.  $\Delta z$ -score was calculated as follows: (z-score in U treatment - z-score in control)

| Locus ID | Symbol | Name  | Category                                    | $\Delta z$ |
|----------|--------|---|---|------------|
| GSU3424  |        | dihydrolipoamide dehydrogenase-related protein  | Cellular processes, Detoxification          | 1.78       |
| GSU1158  | sodA   | superoxide dismutase, iron/manganese-containing | Cellular processes, Detoxification          | 1.72       |
| GSU2212  | cheY-5 | chemotaxis protein CheY                         | Cellular processes, Chemotaxis and motility | 1.71       |
| GSU0582  |        | methyl-accepting chemotaxis protein             | Cellular processes, Chemotaxis and motility | 1.70       |
| GSU0865  |        | cell division protein DivIVA, putative          | Cellular processes, Cell division           | 1.66       |

|         |        |   |  |      |
|---------|--------|---|--|------|
| GSU0352 | prx-3  | peroxiredoxin, atypical 2-Cys subfamily     | Cellular processes, Detoxification                     | 1.66 |
| GSU1905 |        | cold shock domain family protein            | Cellular processes, Adaptations to atypical conditions | 1.58 |
| GSU0099 | mgIA   | cell polarity determinant GTPase MglA       | Cellular processes, Chemotaxis and motility            | 1.55 |
| GSU3199 | cheA-3 | chemotaxis sensor histidine kinase CheA     | Cellular processes, Chemotaxis and motility            | 1.53 |
| GSU0581 |        | cold-shock domain family protein            | Cellular processes, Adaptations to atypical conditions | 1.38 |
| GSU1180 | ftsH-1 | cell division protein FtsH                  | Cellular processes, Cell division                      | 1.35 |
| GSU2220 | cheW-7 | chemotaxis protein CheW                     | Cellular processes, Chemotaxis and motility            | 1.26 |
| GSU2100 | katG   | catalase/peroxidase                         | Cellular processes, Detoxification                     | 1.23 |
| GSU1141 |        | methyl-accepting chemotaxis protein         | Cellular processes, Chemotaxis and motility            | 1.23 |
| GSU0394 |        | AcrB/AcrD/AcrF family protein               | Cellular processes, Toxin production and resistance    | 1.19 |
| GSU3198 | cheY-7 | chemotaxis protein CheY                     | Cellular processes, Chemotaxis and motility            | 1.14 |
| GSU3064 | ftsA   | cell division protein FtsA                  | Cellular processes, Cell division                      | 1.12 |
| GSU2367 |        | organic solvent tolerance protein, putative | Cellular processes, Detoxification                     | 1.06 |
| GSU1832 | scpA   | segregation and condensation protein A      | Cellular processes, Cell division                      | 0.78 |

|         |        |   |  |       |
|---------|--------|---|--|-------|
| GSU1492 | pilT-4 | twitching motility protein PilT               | Cellular processes, Chemotaxis and motility            | 0.58  |
| GSU2657 |        | spore coat protein A                          | Cellular processes, Sporulation and germination        | 0.51  |
| GSU1118 |        | universal stress protein family               | Cellular processes, Adaptations to atypical conditions | -0.26 |
| GSU0191 |        | cold-shock domain family protein              | Cellular processes, Adaptations to atypical conditions | -0.41 |
| GSU1013 |        | chemotaxis MotB protein, putative             | Cellular processes, Chemotaxis and motility            | -0.41 |
| GSU3196 |        | methyl-accepting chemotaxis protein           | Cellular processes, Chemotaxis and motility            | -0.50 |
| GSU1899 |        | virulence factor Mce family protein           | Cellular processes, Pathogenesis                       | -0.55 |
| GSU1704 |        | methyl-accepting chemotaxis protein, putative | Cellular processes, Chemotaxis and motility            | -0.64 |
| GSU0400 |        | methyl-accepting chemotaxis protein           | Cellular processes, Chemotaxis and motility            | -0.66 |
| GSU0401 |        | methyl-accepting chemotaxis protein, putative | Cellular processes, Chemotaxis and motility            | -0.66 |
| GSU0756 |        | methyl-accepting chemotaxis protein           | Cellular processes, Chemotaxis and motility            | -0.66 |
| GSU0916 |        | methyl-accepting chemotaxis protein           | Cellular processes, Chemotaxis and motility            | -0.66 |
| GSU0935 |        | methyl-accepting chemotaxis protein, putative | Cellular processes, Chemotaxis and motility            | -0.66 |
| GSU1029 |        | methyl-accepting chemotaxis protein           | Cellular processes, Chemotaxis and motility            | -0.66 |



|         |        |   |  |       |
|---------|--------|---|--|-------|
| GSU1032 |        | methyl-accepting chemotaxis protein           | Cellular processes, Chemotaxis and motility            | -0.66 |
| GSU1035 |        | methyl-accepting chemotaxis protein           | Cellular processes, Chemotaxis and motility            | -0.66 |
| GSU1041 |        | methyl-accepting chemotaxis protein           | Cellular processes, Chemotaxis and motility            | -0.66 |
| GSU1374 | hylB   | methyl-accepting chemotaxis protein           | Cellular processes, Chemotaxis and motility            | -0.66 |
| GSU2579 |        | methyl-accepting chemotaxis protein           | Cellular processes, Chemotaxis and motility            | -0.66 |
| GSU2652 |        | methyl-accepting chemotaxis protein           | Cellular processes, Chemotaxis and motility            | -0.66 |
| GSU2942 |        | methyl-accepting chemotaxis protein           | Cellular processes, Chemotaxis and motility            | -0.66 |
| GSU3156 |        | methyl-accepting chemotaxis protein, putative | Cellular processes, Chemotaxis and motility            | -0.66 |
| GSU3200 |        | chemotaxis protein, CheC family               | Cellular processes, Chemotaxis and motility            | -0.70 |
| GSU0750 |        | methyl-accepting chemotaxis protein, putative | Cellular processes, Chemotaxis and motility            | -0.70 |
| GSU0583 |        | methyl-accepting chemotaxis protein           | Cellular processes, Chemotaxis and motility            | -0.73 |
| GSU1768 |        | ParA family protein                           | Cellular processes, Cell division                      | -0.77 |
| GSU1809 | ftsH-2 | cell division protein FtsH                    | Cellular processes, Cell division                      | -0.85 |
| GSU0207 |        | cold-shock domain family protein              | Cellular processes, Adaptations to atypical conditions | -0.87 |
| GSU1030 |        | methyl-accepting chemotaxis                   | Cellular processes, Chemotaxis                         | -0.91 |

|         |      |   |  |       |
|---------|------|---|--|-------|
|         |      | protein   | and motility   |       |
| GSU0766 |      | methyl-accepting chemotaxis protein, putative                       | Cellular processes, Chemotaxis and motility            | -0.97 |
| GSU0098 |      | MglB protein  | Cellular processes, Chemotaxis and motility            | -1.05 |
| GSU1408 |      | ParA family protein   | Cellular processes, Cell division                      | -1.06 |
| GSU0515 |      | universal stress protein family                                     | Cellular processes, Adaptations to atypical conditions | -1.09 |
| GSU1214 |      | tetracenomycin polyketide synthesis 8-o-methyltransferase, putative | Cellular processes, Toxin production and resistance    | -1.10 |
| GSU1033 |      | methyl-accepting chemotaxis protein                                 | Cellular processes, Chemotaxis and motility            | -1.14 |
| GSU2550 | drpA | DNA processing protein DprA   | Cellular processes, DNA transformation                 | -1.15 |
| GSU2236 | relA | GTP pyrophosphokinase   | Cellular processes, Adaptations to atypical conditions | -1.25 |
| GSU1130 |      | chromosome segregation SMC protein, putative                        | Cellular processes, Cell division                      | -1.28 |
| GSU3112 |      | cell division protein FtsK, putative                                | Cellular processes, Cell division                      | -1.31 |
| GSU3063 | ftsZ | cell division protein FtsZ  | Cellular processes, Cell division                      | -1.40 |
| GSU2302 |      | trehalose-phosphatase, putative                                     | Cellular processes, Adaptations to atypical conditions | -1.43 |
| GSU2794 | mscL | large conductance   | Cellular processes,                                    | -1.44 |

|         |        |  |  |       |
|---------|--------|--|--|-------|
|         |        | mechanosensitive channel protein                         | Adaptations to atypical conditions                     |       |
| GSU2222 | cheA-2 | chemotaxis protein CheA                                  | Cellular processes, Chemotaxis and motility            | -1.45 |
| GSU0326 | gspG   | general secretion pathway protein G                      | Cellular processes, Pathogenesis                       | -1.48 |
| GSU2372 | mcp028 | methyl-accepting chemotaxis sensory transducer, putative | Cellular processes, Chemotaxis and motility            | -1.53 |
| GSU1304 | mcp025 | methyl-accepting chemotaxis sensory transducer           | Cellular processes, Chemotaxis and motility            | -1.75 |
| GSU2335 | usp-4  | universal stress protein Usp                             | Cellular processes, Adaptations to atypical conditions | -1.81 |

Table B11:  $\Delta z$ -score of proteins involved in amino acid biosynthesis.  $\Delta z$ -score was calculated as follows: (z-score in U treatment - z-score in control)

| Locus ID | Symbol | Name                                    | Category                                  | $\Delta z$ |
|----------|--------|---|---|------------|
| GSU1183  |        | O-acetyl-L-homoserine sulfhydrylase     | Amino acid biosynthesis, Aspartate family | 1.80       |
| GSU1530  | hisG-1 | ATP phosphoribosyltransferase           | Amino acid biosynthesis, Histidine family | 1.77       |
| GSU0160  | dapB   | dihydrodipicolinate reductase           | Amino acid biosynthesis, Aspartate family | 1.77       |
| GSU2425  |        | O-acetyl-L-homoserine sulfhydrylase     | Amino acid biosynthesis, Aspartate family | 1.74       |
| GSU1909  | ilvC   | ketol-acid reductoisomerase             | Amino acid biosynthesis, Pyruvate family  | 1.66       |
| GSU3094  | hisE   | phosphoribosyl-ATP pyrophosphohydrolase | Amino acid biosynthesis, Histidine family | 1.63       |
| GSU0152  | argF   | ornithine carbamoyltransferase          | Amino acid biosynthesis, Glutamate family | 1.61       |

|         |        |   |  |      |
|---------|--------|---|--|------|
| GSU2572 | cysE   | serine acetyltransferase  | Amino acid biosynthesis,<br>Serine family              | 1.60 |
| GSU0156 | argH   | argininosuccinate lyase   | Amino acid biosynthesis,<br>Glutamate family           | 1.60 |
| GSU2383 | trpE   | anthranilate synthase<br>component I  | Amino acid biosynthesis,<br>Aromatic amino acid family | 1.59 |
| GSU0150 | argB   | acetylglutamate kinase  | Amino acid biosynthesis,<br>Glutamate family           | 1.56 |
| GSU0153 | argG   | argininosuccinate synthase  | Amino acid biosynthesis,<br>Glutamate family           | 1.55 |
| GSU1242 | aatA   | aspartate aminotransferase  | Amino acid biosynthesis,<br>Aspartate family           | 1.52 |
| GSU0656 | ilvE   | branched-chain amino acid<br>aminotransferase                                   | Amino acid biosynthesis,<br>Pyruvate family            | 1.41 |
| GSU3101 | hisG-2 | ATP<br>phosphoribosyltransferase  | Amino acid biosynthesis,<br>Histidine family           | 1.36 |
| GSU3057 | gltA   | glutamate synthase (NADPH),<br>homotetrameric                                   | Amino acid biosynthesis,<br>Glutamate family           | 1.31 |
| GSU0535 | cysK   | cysteine synthase A   | Amino acid biosynthesis,<br>Serine family              | 1.17 |
| GSU0945 | metC-2 | cystathionine beta-lyase  | Amino acid biosynthesis,<br>Aspartate family           | 1.16 |
| GSU1906 | leuA   | 2-isopropylmalate synthase  | Amino acid biosynthesis,<br>Pyruvate family            | 1.11 |
| GSU3097 | hisH   | imidazole glycerol phosphate<br>synthase, glutamine<br>amidotransferase subunit | Amino acid biosynthesis,<br>Histidine family           | 1.09 |
| GSU1799 |        | aspartate kinase,<br>monofunctional class                                       | Amino acid biosynthesis,<br>Aspartate family           | 1.06 |
| GSU3158 | cysM   | cysteine synthase B   | Amino acid biosynthesis,                               | 0.91 |

|         |      |  |   |       |
|---------|------|--|---|-------|
|         |      |  | Serine family                                       |       |
| GSU3098 | hisB | imidazoleglycerol-phosphate dehydratase                    | Amino acid biosynthesis, Histidine family           | 0.90  |
| GSU1695 | thrC | threonine synthase   | Amino acid biosynthesis, Aspartate family           | 0.88  |
| GSU1820 |      | protein-P-II uridylyltransferase, putative                 | Amino acid biosynthesis, Glutamate family           | 0.81  |
| GSU0151 | argD | acetylornithine aminotransferase                           | Amino acid biosynthesis, Glutamate family           | 0.81  |
| GSU1953 | asnB | asparagine synthase, glutamine-hydrolyzing                 | Amino acid biosynthesis, Aspartate family           | 0.78  |
| GSU0159 | dapA | dihydrodipicolinate synthase                               | Amino acid biosynthesis, Aspartate family           | 0.73  |
| GSU2606 | aroA | 3-phosphoshikimate 1-carboxyvinyltransferase               | Amino acid biosynthesis, Aromatic amino acid family | 0.66  |
| GSU2049 | argJ | glutamate N-acetyltransferase/amino-acid acetyltransferase | Amino acid biosynthesis, Glutamate family           | 0.55  |
| GSU2025 | aroB | 3-dehydroquinate synthase                                  | Amino acid biosynthesis, Aromatic amino acid family | 0.47  |
| GSU1902 |      | 3-isopropylmalate dehydratase, small subunit, putative     | Amino acid biosynthesis, Pyruvate family            | 0.47  |
| GSU2541 | proC | pyrroline-5-carboxylate reductase                          | Amino acid biosynthesis, Glutamate family           | 0.27  |
| GSU1198 | serA | D-3-phosphoglycerate dehydrogenase                         | Amino acid biosynthesis, Serine family              | 0.26  |
| GSU0531 | dapF | diaminopimelate epimerase                                  | Amino acid biosynthesis, Aspartate family           | 0.06  |
| GSU2371 | trpA | tryptophan synthase, alpha subunit                         | Amino acid biosynthesis, Aromatic amino acid family | -0.17 |

|         |        |   |  |       |
|---------|--------|---|--|-------|
| GSU3142 |        | phospho-2-dehydro-3-deoxyheptonate aldolase                             | Amino acid biosynthesis,<br>Aromatic amino acid family | -0.20 |
| GSU2291 |        | phospho-2-dehydro-3-deoxyheptonate aldolase                             | Amino acid biosynthesis,<br>Aromatic amino acid family | -0.22 |
| GSU0158 | lysA   | diaminopimelate decarboxylase   | Amino acid biosynthesis,<br>Aspartate family           | -0.23 |
| GSU1903 |        | 3-isopropylmalate dehydratase, large subunit, putative                  | Amino acid biosynthesis,<br>Pyruvate family            | -0.35 |
| GSU1607 | glyA   | serine hydroxymethyltransferase   | Amino acid biosynthesis,<br>Serine family              | -0.44 |
| GSU2879 | leuB   | 3-isopropylmalate dehydrogenase   | Amino acid biosynthesis,<br>Pyruvate family            | -0.59 |
| GSU3333 |        | phospho-2-dehydro-3-deoxyheptonate aldolase                             | Amino acid biosynthesis,<br>Aromatic amino acid family | -0.63 |
| GSU3096 | hisA   | phosphoribosylformimino-5-aminoimidazole carboxamide ribotide isomerase | Amino acid biosynthesis,<br>Histidine family           | -0.64 |
| GSU2874 | argC   | N-acetyl-gamma-glutamyl-phosphate reductase                             | Amino acid biosynthesis,<br>Glutamate family           | -0.64 |
| GSU3260 |        | phosphoserine aminotransferase, putative                                | Amino acid biosynthesis,<br>Serine family              | -0.74 |
| GSU3211 | proA   | gamma-glutamyl phosphate reductase                                      | Amino acid biosynthesis,<br>Glutamate family           | -0.87 |
| GSU0215 | fold-1 | fold bifunctional protein   | Amino acid biosynthesis,<br>Aspartate family           | -0.96 |
| GSU2379 |        | pyridoxal-phosphate dependent enzyme                                    | Amino acid biosynthesis,<br>Aromatic amino acid family | -1.00 |
| GSU3100 | hisD   | histidinol dehydrogenase  | Amino acid biosynthesis,<br>Histidine family           | -1.02 |
| GSU0484 | tdcB   | threonine and serine  | Amino acid biosynthesis,                               | -1.07 |

|         |        |   |  |       |
|---------|--------|---|--|-------|
|         |        | dehydratase and deaminase,<br>catabolic                         | Pyruvate family  |       |
| GSU2539 | LYS1   | saccharopine dehydrogenase                                      | Amino acid biosynthesis,<br>Aspartate family           | -1.14 |
| GSU1693 | hom    | homoserine dehydrogenase  | Amino acid biosynthesis,<br>Aspartate family           | -1.14 |
| GSU1912 | ilvD   | dihydroxy-acid dehydratase                                      | Amino acid biosynthesis,<br>Pyruvate family            | -1.26 |
| GSU2608 | pheA   | chorismate mutase/prephenate<br>dehydratase                     | Amino acid biosynthesis,<br>Aromatic amino acid family | -1.31 |
| GSU1910 | ilvN   | acetolactate synthase, small<br>subunit                         | Amino acid biosynthesis,<br>Pyruvate family            | -1.34 |
| GSU0944 | metC-1 | cystathionine beta-lyase  | Amino acid biosynthesis,<br>Aspartate family           | -1.36 |
| GSU1835 | glnA   | glutamine synthetase, type I                                    | Amino acid biosynthesis,<br>Glutamate family           | -1.37 |
| GSU2878 |        | aspartate-semialdehyde<br>dehydrogenase, putative               | Amino acid biosynthesis,<br>Aspartate family           | -1.45 |
| GSU1531 | hisI   | phosphoribosyl-AMP<br>cyclohydrolase                            | Amino acid biosynthesis,<br>Histidine family           | -1.46 |
| GSU0486 | ilvA   | threonine dehydratase   | Amino acid biosynthesis,<br>Pyruvate family            | -1.49 |
| GSU1061 |        | aspartate aminotransferase                                      | Amino acid biosynthesis,<br>Aspartate family           | -1.53 |
| GSU2921 | metH   | 5-methyltetrahydrofolate--<br>homocysteine<br>methyltransferase | Amino acid biosynthesis,<br>Aspartate family           | -1.60 |
| GSU3099 | hisC   | histidinol-phosphate<br>aminotransferase                        | Amino acid biosynthesis,<br>Histidine family           | -1.63 |
| GSU3095 | hisF   | imidazoleglycerol phosphate                                     | Amino acid biosynthesis,                               | -1.64 |

|         |      |  |  |       |
|---------|------|--|--|-------|
|         |      | synthase, cyclase subunit                                  | Histidine family                                       |       |
| GSU1828 |      | chorismate mutase  | Amino acid biosynthesis,<br>Aromatic amino acid family | -1.66 |
| GSU1911 | ilvB | acetolactate synthase, large<br>subunit, biosynthetic type | Amino acid biosynthesis,<br>Pyruvate family            | -1.71 |

Table B12:  $\Delta z$ -score of proteins involved in cell envelope metabolism.  $\Delta z$ -score was calculated as follows: (z-score in U treatment - z-score in control)

| Locus ID | Symbol | Name  | Category   | $\Delta z$ |
|----------|--------|---|--|------------|
| GSU1493  | pilC   | type IV pilus biogenesis<br>protein PilC  | Cell envelope, Surface<br>structures   | 1.79       |
| GSU1817  |        | outer membrane lipoprotein,<br>Slp family   | Cell envelope, Other   | 1.79       |
| GSU0457  |        | outer membrane lipoprotein<br>LolB, putative  | Cell envelope, Other   | 1.76       |
| GSU3066  | ddl    | D-alanine--D-alanine ligase   | Cell envelope, Biosynthesis<br>and degradation of murein<br>sacculus and peptidoglycan | 1.74       |
| GSU3072  | murF   | UDP-N-<br>acetylmuramoylalanyl-D-<br>glutamyl-2,6-diaminopimelate-<br>D-alanyl-D-alanyl ligase,<br>frameshifted | Cell envelope, Other   | 1.70       |
| GSU2923  | murI   | glutamate racemase  | Cell envelope, Biosynthesis<br>and degradation of murein<br>sacculus and peptidoglycan | 1.66       |
| GSU2431  | nfeD   | NfeD-like membrane-bound<br>serine protease   | Cell envelope, Other   | 1.57       |
| GSU2029  | pilP   | type IV pilus assembly  | Cell envelope, Other   | 1.55       |



|         |      |  |  |      |
|---------|------|--|--|------|
|         |      | lipoprotein PilP, putative                       |  |      |
| GSU2028 | pilQ | type IV pilus biogenesis protein PilQ            | Cell envelope, Surface structures  | 1.50 |
| GSU2089 | mreB | rod shape-determining protein MreB               | Cell envelope, Biosynthesis and degradation of murein sacculus and peptidoglycan | 1.50 |
| GSU0427 |      | lipoprotein, putative                            | Cell envelope, Other   | 1.49 |
| GSU3133 |      | penicillin-binding protein, 1A family            | Cell envelope, Biosynthesis and degradation of murein sacculus and peptidoglycan | 1.48 |
| GSU0543 |      | outer membrane lipoprotein, Slp family, putative | Cell envelope, Other   | 1.47 |
| GSU2081 | mreC | rod shape-determining protein MreC               | Cell envelope, Biosynthesis and degradation of murein sacculus and peptidoglycan | 1.39 |
| GSU2458 |      | penicillin-binding protein, putative             | Cell envelope, Biosynthesis and degradation of murein sacculus and peptidoglycan | 1.35 |
| GSU3466 |      | membrane protein, putative                       | Cell envelope, Other   | 1.33 |
| GSU2498 |      | lipoprotein, putative                            | Cell envelope, Other   | 1.26 |
| GSU0872 |      | lipoprotein, putative                            | Cell envelope, Other   | 1.03 |
| GSU0636 |      | membrane protein, putative                       | Cell envelope, Other   | 0.89 |
| GSU3068 | murC | UDP-N-acetylmuramate--alanine ligase             | Cell envelope, Biosynthesis and degradation of murein sacculus and peptidoglycan | 0.87 |
| GSU2030 |      | type IV pilus biogenesis protein PilO            | Cell envelope, Surface structures  | 0.87 |
| GSU2305 |      | peptidoglycan-associated lipoprotein             | Cell envelope, Other   | 0.85 |
| GSU1489 |      | membrane protein, putative                       | Cell envelope, Other   | 0.58 |

|         |      |  |  |       |
|---------|------|--|--|-------|
| GSU2208 |      | lipoprotein, putative  | Cell envelope, Other   | 0.56  |
| GSU2268 |      | outer membrane protein, putative                                 | Cell envelope, Other   | 0.48  |
| GSU1805 | glmM | phosphoglucosamine mutase  | Cell envelope, Biosynthesis and degradation of murein sacculus and peptidoglycan | 0.35  |
| GSU1091 |      | lipoprotein, putative  | Cell envelope, Other   | 0.30  |
| GSU2333 |      | membrane protein, putative                                       | Cell envelope, Other   | 0.26  |
| GSU3074 | murE | UDP-N-acetylmuramoylalanyl-D-glutamyl-2,6-diaminopimelate ligase | Cell envelope, Biosynthesis and degradation of murein sacculus and peptidoglycan | 0.13  |
| GSU0456 |      | membrane protein, putative                                       | Cell envelope, Other   | 0.11  |
| GSU0501 |      | lipoprotein, putative  | Cell envelope, Other   | -0.06 |
| GSU1783 |      | type IV pilus biogenesis protein PilB, putative                  | Cell envelope, Surface structures  | -0.15 |
| GSU2277 |      | lipoprotein, NLP/P60 family, putative                            | Cell envelope, Other   | -0.16 |
| GSU2552 |      | lipoprotein, putative  | Cell envelope, Other   | -0.18 |
| GSU0622 |      | membrane protein, putative                                       | Cell envelope, Other   | -0.18 |
| GSU2272 |      | lipoprotein, putative  | Cell envelope, Other   | -0.21 |
| GSU2267 |      | outer membrane protein, putative                                 | Cell envelope, Other   | -0.22 |
| GSU1491 |      | type IV pilus biogenesis protein PilB                            | Cell envelope, Surface structures  | -0.35 |
| GSU2031 |      | type IV pilus biogenesis protein PilN                            | Cell envelope, Surface structures  | -0.37 |
| GSU1922 |      | membrane protein, putative                                       | Cell envelope, Other   | -0.44 |
| GSU0182 |      | lipoprotein, putative  | Cell envelope, Other   | -0.48 |
| GSU3462 |      | lipoprotein, putative  | Cell envelope, Other   | -0.66 |

|         |      |   |  |       |
|---------|------|---|--|-------|
| GSU0271 | glmU | UDP-N-acetylglucosamine pyrophosphorylase   | Cell envelope, Biosynthesis and degradation of murein sacculus and peptidoglycan | -0.70 |
| GSU1869 |      | lipoprotein, putative   | Cell envelope, Other   | -0.73 |
| GSU3102 | murA | UDP-N-acetylglucosamine 1-carboxyvinyltransferase   | Cell envelope, Biosynthesis and degradation of murein sacculus and peptidoglycan | -0.84 |
| GSU3130 |      | lipoprotein, putative   | Cell envelope, Other   | -0.85 |
| GSU3069 | murG | UDP-N-acetylglucosamine--N-acetylmuramyl-(pentapeptide) pyrophosphoryl-undecaprenol N-acetylglucosamine transferase | Cell envelope, Biosynthesis and degradation of murein sacculus and peptidoglycan | -0.92 |
| GSU0381 |      | lipoprotein, putative   | Cell envelope, Other   | -0.94 |
| GSU1984 |      | polysaccharide chain length determinant protein, putative   | Cell envelope, Other   | -1.02 |
| GSU2104 |      | lipoprotein, putative   | Cell envelope, Other   | -1.06 |
| GSU2032 |      | type IV pilus biogenesis protein PilM   | Cell envelope, Surface structures  | -1.07 |
| GSU2940 |      | lipoprotein, putative   | Cell envelope, Other   | -1.12 |
| GSU1229 |      | lipoprotein, putative   | Cell envelope, Other   | -1.22 |
| GSU3071 | murD | UDP-N-acetylmuramoylalanine--D-glutamate ligase   | Cell envelope, Biosynthesis and degradation of murein sacculus and peptidoglycan | -1.29 |
| GSU2633 |      | lipoprotein, putative   | Cell envelope, Other   | -1.30 |
| GSU1153 |      | outer membrane protein, OMP85 family  | Cell envelope, Other   | -1.38 |
| GSU0733 |      | cell shape-determining protein MreB/Mrl family  | Cell envelope, Biosynthesis and degradation of murein sacculus and peptidoglycan | -1.41 |

|         |  |                       |                      |       |
|---------|--|-----------------------|----------------------|-------|
| GSU0183 |  | lipoprotein, putative | Cell envelope, Other | -1.43 |
| GSU3314 |  | lipoprotein, putative | Cell envelope, Other | -1.50 |
| GSU1743 |  | lipoprotein, putative | Cell envelope, Other | -1.58 |
| GSU2973 |  | lipoprotein, putative | Cell envelope, Other | -1.63 |

Table B13:  $\Delta z$ -score of proteins involved in central intermediary metabolism.  $\Delta z$ -score was calculated as follows: (z-score in U treatment - z-score in control)

| Locus ID | Symbol | Name  | Category  | $\Delta z$ |
|----------|--------|---|---|------------|
| GSU2821  | nifH   | nitrogenase iron protein                                    | Central intermediary metabolism, Nitrogen fixation      | 1.75       |
| GSU2538  | nspC   | carboxynorspermidine decarboxylase                          | Central intermediary metabolism, Polyamine biosynthesis | 1.71       |
| GSU1875  | ahcY   | S-adenosyl-L-homocysteine hydrolase                         | Central intermediary metabolism, One-carbon metabolism  | 1.65       |
| GSU2559  |        | exopolyphosphatase  | Central intermediary metabolism, Phosphorus compounds   | 1.64       |
| GSU2012  | nifU   | nitrogen fixation iron-sulfur cluster assembly protein NifU | Central intermediary metabolism, Nitrogen fixation      | 1.59       |
| GSU3265  |        | sulfite reductase, assimilatory-type                        | Central intermediary metabolism, Sulfur metabolism      | 1.56       |
| GSU1028  |        | peptidylarginine deiminase-related protein                  | Central intermediary metabolism, Amino sugars           | 1.47       |
| GSU0910  |        | aldehyde:ferredoxin oxidoreductase, tungsten-containing     | Central intermediary metabolism, Other                  | 1.42       |
| GSU2307  |        | carbonic anhydrase  | Central intermediary metabolism, Other                  | 1.18       |

|         |       |  |   |       |
|---------|-------|--|---|-------|
| GSU1716 |       | phosphoadenosine phosphosulfate reductase, putative              | Central intermediary metabolism, Sulfur metabolism      | 1.17  |
| GSU0809 |       | carbonic anhydrase, putative                                     | Central intermediary metabolism, Other                  | 1.16  |
| GSU2819 | nifK  | nitrogenase molybdenum-iron protein, beta subunit                | Central intermediary metabolism, Nitrogen fixation      | 0.89  |
| GSU2820 | nifD  | nitrogenase molybdenum-iron protein, alpha chain                 | Central intermediary metabolism, Nitrogen fixation      | 0.86  |
| GSU1880 | metK  | S-adenosylmethionine synthetase                                  | Central intermediary metabolism, Other                  | 0.68  |
| GSU2806 | nifEN | nitrogenase molybdenum-iron cofactor biosynthesis protein NifEN  | Central intermediary metabolism, Nitrogen fixation      | 0.66  |
| GSU2803 |       | dinitrogenase iron-molybdenum cofactor family protein            | Central intermediary metabolism, Nitrogen fixation      | 0.64  |
| GSU1672 | hprA  | glycerate dehydrogenase  | Central intermediary metabolism, Other                  | 0.29  |
| GSU1027 |       | glycosyl hydrolase, family 10                                    | Central intermediary metabolism, Nitrogen metabolism    | 0.19  |
| GSU2975 |       | inorganic pyrophosphatase, manganese-dependent, putative         | Central intermediary metabolism, Phosphorus compounds   | -0.48 |
| GSU0270 | glmS  | glucosamine--fructose-6-phosphate aminotransferase (isomerizing) | Central intermediary metabolism, Amino sugars           | -0.82 |
| GSU2537 | speA  | biosynthetic arginine decarboxylase                              | Central intermediary metabolism, Polyamine biosynthesis | -1.02 |

|         |      |   |   |       |
|---------|------|---|---|-------|
| GSU0453 | pfs  | MTA/SAH nucleosidase                                    | Central intermediary metabolism, Other                  | -1.10 |
| GSU3323 | ppk  | polyphosphate kinase                                    | Central intermediary metabolism, Phosphorus compounds   | -1.19 |
| GSU1717 | cysD | sulfate adenylyltransferase, subunit 2                  | Central intermediary metabolism, Sulfur metabolism      | -1.48 |
| GSU2191 |      | aldehyde ferredoxin oxidoreductase, tungsten-containing | Central intermediary metabolism, Other                  | -1.65 |
| GSU2502 |      | spermine/spermidine synthase family protein             | Central intermediary metabolism, Polyamine biosynthesis | -1.80 |

Table B14:  $\Delta z$ -score of proteins with unknown function.  $\Delta z$ -score was calculated as follows: (z-score in U treatment - z-score in control)

| Locus ID | Symbol | Name  | Category   | $\Delta z$ |
|----------|--------|---|--|------------|
| GSU2213  |        | GAF domain protein                                    | Unknown function, General                        | 1.82       |
| GSU2429  |        | peptidylprolyl cis-trans isomerase, PpiC-type         | Unknown function, General                        | 1.82       |
| GSU0014  |        | DnaJ-related molecular chaperone                      | Unknown function, General                        | 1.82       |
| GSU1458  |        | TPR domain protein                                    | Unknown function, General                        | 1.80       |
| GSU3077  | mraW   | SAM-dependent membrane protein methyltransferase MraW | Unknown function, Enzymes of unknown specificity | 1.78       |
| GSU2516  |        | rhodanese homology domain pair                        | Unknown function,                                | 1.77       |

|         |      |   |  |      |
|---------|------|---|--|------|
|         |      | protein   | General  |      |
| GSU0197 |      | oxidoreductase, short chain dehydrogenase/reductase family                                      | Unknown function, Enzymes of unknown specificity | 1.76 |
| GSU1090 |      | signal transduction protein-related protein, response receiver                                  | Unknown function, General                        | 1.76 |
| GSU2062 |      | response receiver-modulated nucleotide cyclase, GGDEF-related domain-containing                 | Unknown function, General                        | 1.72 |
| GSU0869 |      | LysM domain/NLP/P60 family protein  | Unknown function, General                        | 1.69 |
| GSU2477 |      | cobalamin-binding radical SAM domain iron-sulfur cluster-binding oxidoreductase with TPR domain | Unknown function, General                        | 1.69 |
| GSU3209 |      | protein of unknown function DUF143  | Unknown function, General                        | 1.68 |
| GSU0505 |      | rhodanese homology domain superfamily protein   | Unknown function, General                        | 1.66 |
| GSU0157 |      | lipoprotein, putative   | Unknown function, General                        | 1.65 |
| GSU3454 |      | radical SAM domain iron-sulfur cluster-binding oxidoreductase                                   | Unknown function, Enzymes of unknown specificity | 1.64 |
| GSU0585 | ycgM | fumarylacetoacetate hydrolase family protein ycgM   | Unknown function, Enzymes of unknown specificity | 1.63 |
| GSU2493 |      | NHL repeat domain protein   | Unknown function, General                        | 1.63 |
| GSU1614 |      | CoA-binding protein   | Unknown function, General                        | 1.62 |

|         |      |  |  |      |
|---------|------|--|--|------|
| GSU1708 |      | metal-dependent hydrolase,<br>subgroup D             | Unknown function,<br>Enzymes of unknown<br>specificity | 1.60 |
| GSU0361 |      | peptidylprolyl cis-trans isomerase,<br>PpiC-type     | Unknown function,<br>General                           | 1.59 |
| GSU1432 |      | TPR domain protein                                   | Unknown function,<br>General                           | 1.55 |
| GSU1222 |      | histone deacetylase family protein                   | Unknown function,<br>General                           | 1.54 |
| GSU2583 | ycaC | isochorismatase family protein<br>YcaC               | Unknown function,<br>Enzymes of unknown<br>specificity | 1.52 |
| GSU0617 |      | NHL repeat domain lipoprotein                        | Unknown function,<br>General                           | 1.51 |
| GSU0644 |      | RNA-binding KH domain protein,<br>putative           | Unknown function,<br>General                           | 1.51 |
| GSU2610 |      | LysM domain protein                                  | Unknown function,<br>General                           | 1.49 |
| GSU3145 |      | MOSC domain protein                                  | Unknown function,<br>General                           | 1.49 |
| GSU1877 |      | oxidoreductase, 2-nitropropane<br>dioxygenase family | Unknown function,<br>Enzymes of unknown<br>specificity | 1.49 |
| GSU1327 |      | homocysteine S-methyltransferase<br>domain protein   | Unknown function,<br>General                           | 1.48 |
| GSU0434 |      | ThiI family protein                                  | Unknown function,<br>General                           | 1.47 |
| GSU2476 |      | TPR domain protein                                   | Unknown function,<br>General                           | 1.47 |
| GSU2888 |      | B12-binding domain                                   | Unknown function,                                      | 1.46 |



|         |  |   |   |      |
|---------|--|---|---|------|
|         |  | protein/radical SAM domain protein                                    | General   |      |
| GSU1306 |  | PHP domain protein  | Unknown function,<br>General                        | 1.45 |
| GSU0016 |  | PPIC-type PPIASE domain protein                                       | Unknown function,<br>General                        | 1.44 |
| GSU1818 |  | phosphoglycerate mutase family protein                                | Unknown function,<br>Enzymes of unknown specificity | 1.43 |
| GSU0876 |  | diacylglycerol kinase catalytic domain protein                        | Unknown function,<br>General                        | 1.40 |
| GSU1149 |  | EAL domain protein  | Unknown function,<br>General                        | 1.39 |
| GSU2555 |  | dolichyl-phosphate-mannose-protein mannosyltransferase family protein | Unknown function,<br>General                        | 1.38 |
| GSU1997 |  | PDZ domain protein  | Unknown function,<br>General                        | 1.37 |
| GSU1801 |  | CBS domain protein  | Unknown function,<br>General                        | 1.36 |
| GSU1371 |  | oxidoreductase, FAD/FMN-binding                                       | Unknown function,<br>Enzymes of unknown specificity | 1.36 |
| GSU1123 |  | metallo-beta-lactamase family protein                                 | Unknown function,<br>Enzymes of unknown specificity | 1.36 |
| GSU3277 |  | lysM domain protein   | Unknown function,<br>General                        | 1.35 |
| GSU3240 |  | radical SAM domain protein  | Unknown function,<br>Enzymes of unknown             | 1.35 |

|         |  |   |  |      |
|---------|--|---|--|------|
|         |  |   | specificity  |      |
| GSU0235 |  | S1 RNA binding domain protein                                   | Unknown function,<br>General                           | 1.33 |
| GSU3330 |  | NADH-dependent flavin<br>oxidoreductase, Oye family             | Unknown function,<br>Enzymes of unknown<br>specificity | 1.29 |
| GSU1237 |  | pyridine nucleotide-disulphide<br>oxidoreductase family protein | Unknown function,<br>Enzymes of unknown<br>specificity | 1.28 |
| GSU1274 |  | radical SAM domain protein                                      | Unknown function,<br>Enzymes of unknown<br>specificity | 1.26 |
| GSU1398 |  | SCO1/SenC family protein  | Unknown function,<br>General                           | 1.26 |
| GSU3343 |  | SpoVR-like family protein                                       | Unknown function,<br>General                           | 1.25 |
| GSU1698 |  | TPR domain protein  | Unknown function,<br>General                           | 1.25 |
| GSU0162 |  | aromatic aminotransferase,<br>putative                          | Unknown function,<br>Enzymes of unknown<br>specificity | 1.18 |
| GSU2430 |  | SPFH/Band 7 domain protein                                      | Unknown function,<br>General                           | 1.16 |
| GSU0527 |  | trkA domain protein   | Unknown function,<br>General                           | 1.12 |
| GSU3157 |  | hydrolase, alpha/beta fold family                               | Unknown function,<br>Enzymes of unknown<br>specificity | 1.08 |
| GSU0217 |  | nitroreductase family protein                                   | Unknown function,<br>Enzymes of unknown                | 1.05 |

|         |      |                                       |  |      |
|---------|------|---------------------------------------|--|------|
|         |      |                                       | specificity                                      |      |
| GSU1925 |      | transport-associated domain protein   | Unknown function, General                        | 1.01 |
| GSU1361 |      | Piwi domain protein                   | Unknown function, General                        | 1.00 |
| GSU2551 |      | LysM domain protein                   | Unknown function, General                        | 0.99 |
| GSU2536 |      | dienelactone hydrolase family protein | Unknown function, Enzymes of unknown specificity | 0.96 |
| GSU2615 |      | TPR domain protein                    | Unknown function, General                        | 0.96 |
| GSU3461 |      | thioesterase family protein           | Unknown function, General                        | 0.90 |
| GSU0015 |      | PPIC-type PPIASE domain protein       | Unknown function, General                        | 0.88 |
| GSU1974 |      | DegT/DnrJ/EryC1/StrS family protein   | Unknown function, General                        | 0.88 |
| GSU1736 |      | ACT domain protein                    | Unknown function, General                        | 0.87 |
| GSU1987 |      | TPR domain protein                    | Unknown function, General                        | 0.86 |
| GSU0029 |      | hydrolase, carbon-nitrogen family     | Unknown function, Enzymes of unknown specificity | 0.85 |
| GSU0664 | ychF | GTP binding protein YchF              | Unknown function, General                        | 0.79 |
| GSU2216 |      | PBS lyase HEAT-like repeat protein    | Unknown function, General                        | 0.76 |
| GSU0817 |      | transporter membrane protein of       | Unknown function,                                | 0.75 |

|         |  |   |   |      |
|---------|--|---|---|------|
|         |  | unknown function DUF140                               | General   |      |
| GSU1137 |  | KH domain/HD domain protein                           | Unknown function,<br>General                        | 0.74 |
| GSU3078 |  | mraZ protein, putative                                | Unknown function,<br>General                        | 0.74 |
| GSU0331 |  | trypsin domain/PDZ domain protein                     | Unknown function,<br>General                        | 0.74 |
| GSU0534 |  | Rrf2 family protein                                   | Unknown function,<br>General                        | 0.70 |
| GSU3299 |  | carboxyl transferase domain protein                   | Unknown function,<br>General                        | 0.70 |
| GSU0273 |  | radical SAM domain protein                            | Unknown function,<br>Enzymes of unknown specificity | 0.70 |
| GSU3450 |  | glutamate synthase-related protein                    | Unknown function,<br>General                        | 0.64 |
| GSU1195 |  | HD domain protein                                     | Unknown function,<br>General                        | 0.63 |
| GSU3300 |  | biotin-requiring enzyme subunit                       | Unknown function,<br>Enzymes of unknown specificity | 0.60 |
| GSU1590 |  | DHH family/DHHA1 domain protein                       | Unknown function,<br>General                        | 0.55 |
| GSU0314 |  | general secretion protein E N-terminal domain protein | Unknown function,<br>General                        | 0.50 |
| GSU1968 |  | nucleotidyltransferase family protein                 | Unknown function,<br>Enzymes of unknown specificity | 0.49 |
| GSU3447 |  | AhpC/TSA family protein                               | Unknown function,<br>General                        | 0.46 |

|         |  |  |   |      |
|---------|--|--|---|------|
| GSU3113 |  | metallo-beta-lactamase family protein              | Unknown function,<br>Enzymes of unknown specificity | 0.46 |
| GSU2745 |  | ATPase, AAA family                                 | Unknown function,<br>General                        | 0.42 |
| GSU3126 |  | oxidoreductase, aldo/keto reductase family         | Unknown function,<br>Enzymes of unknown specificity | 0.40 |
| GSU1677 |  | AMP-binding enzyme/acyltransferase                 | Unknown function,<br>Enzymes of unknown specificity | 0.36 |
| GSU1138 |  | Ser/Thr protein phosphatase family protein         | Unknown function,<br>Enzymes of unknown specificity | 0.35 |
| GSU2974 |  | methylenetetrahydrofolate reductase family protein | Unknown function,<br>Enzymes of unknown specificity | 0.31 |
| GSU0490 |  | acetyl-CoA hydrolase/transferase family protein    | Unknown function,<br>Enzymes of unknown specificity | 0.26 |
| GSU0613 |  | ResB-like family protein                           | Unknown function,<br>General                        | 0.24 |
| GSU1224 |  | TPR domain protein                                 | Unknown function,<br>General                        | 0.23 |
| GSU1937 |  | GGDEF domain/HAMP domain protein                   | Unknown function,<br>General                        | 0.19 |
| GSU3276 |  | LysM domain protein                                | Unknown function,<br>General                        | 0.16 |
| GSU1122 |  | HD domain protein                                  | Unknown function,<br>General                        | 0.16 |

|         |  |   |  |       |
|---------|--|---|--|-------|
| GSU1446 |  | radical SAM domain protein                            | Unknown function,<br>Enzymes of unknown<br>specificity | 0.15  |
| GSU0926 |  | mce-related protein                                   | Unknown function,<br>General                           | 0.15  |
| GSU2010 |  | CBS domain protein                                    | Unknown function,<br>General                           | 0.14  |
| GSU0179 |  | NADPH-dependent FMN<br>reductase domain protein       | Unknown function,<br>General                           | 0.03  |
| GSU2282 |  | CBS domain protein                                    | Unknown function,<br>General                           | -0.06 |
| GSU0174 |  | acetyl-CoA hydrolase/transferase<br>family protein    | Unknown function,<br>Enzymes of unknown<br>specificity | -0.08 |
| GSU1721 |  | radical SAM domain protein                            | Unknown function,<br>Enzymes of unknown<br>specificity | -0.13 |
| GSU2196 |  | hydrolase, putative                                   | Unknown function,<br>Enzymes of unknown<br>specificity | -0.14 |
| GSU1939 |  | GAF domain/His Kinase A<br>domain/HD domain protein   | Unknown function,<br>General                           | -0.15 |
| GSU2527 |  | nitrite/sulfite reductase domain<br>protein           | Unknown function,<br>General                           | -0.17 |
| GSU1982 |  | general secretion pathway protein-<br>related protein | Unknown function,<br>General                           | -0.23 |
| GSU1842 |  | polysaccharide biosynthesis/export<br>domain protein  | Unknown function,<br>General                           | -0.26 |
| GSU2073 |  | EF hand domain/PKD domain<br>protein                  | Unknown function,<br>General                           | -0.29 |

|         |     |   |  |       |
|---------|-----|---|--|-------|
| GSU2547 | gid | gid protein   | Unknown function,<br>General                           | -0.31 |
| GSU3191 |     | TPR domain protein  | Unknown function,<br>General                           | -0.31 |
| GSU1114 |     | TPR domain protein  | Unknown function,<br>General                           | -0.34 |
| GSU1150 |     | oxidative cyclase-related protein                           | Unknown function,<br>General                           | -0.35 |
| GSU1193 |     | ketose-bisphosphate aldolase<br>family protein              | Unknown function,<br>Enzymes of unknown<br>specificity | -0.42 |
| GSU1892 |     | phosphatase, YrbI family                                    | Unknown function,<br>Enzymes of unknown<br>specificity | -0.46 |
| GSU1718 |     | elongation factor Tu GTP binding<br>domain protein          | Unknown function,<br>General                           | -0.50 |
| GSU0480 |     | NifU-like domain protein                                    | Unknown function,<br>General                           | -0.53 |
| GSU1207 |     | HesB/YadR/YfhF family protein,<br>selenocysteine-containing | Unknown function,<br>General                           | -0.53 |
| GSU0651 |     | hydrolase, carbon-nitrogen family                           | Unknown function,<br>Enzymes of unknown<br>specificity | -0.56 |
| GSU2715 |     | fibronectin type III domain protein                         | Unknown function,<br>General                           | -0.57 |
| GSU1537 |     | general secretion pathway protein-<br>related protein       | Unknown function,<br>General                           | -0.57 |
| GSU3435 |     | ankyrin repeat protein                                      | Unknown function,<br>General                           | -0.58 |
| GSU0441 |     | radical SAM domain protein                                  | Unknown function,                                      | -0.59 |

|         |      |   |  |       |
|---------|------|---|--|-------|
|         |      |   | Enzymes of unknown specificity                   |       |
| GSU1587 |      | ribosomal protein L7Ae family protein                       | Unknown function, General                        | -0.61 |
| GSU3000 |      | cbiX protein  | Unknown function, General                        | -0.62 |
| GSU1014 |      | smr domain protein  | Unknown function, General                        | -0.63 |
| GSU3007 |      | phosphoglycerate mutase family, putative                    | Unknown function, Enzymes of unknown specificity | -0.66 |
| GSU0024 |      | OmpA domain protein   | Unknown function, General                        | -0.66 |
| GSU0500 | typA | GTP-binding protein TypA                                    | Unknown function, General                        | -0.67 |
| GSU3378 |      | glutamate-ammonia ligase adenylyltransferase domain protein | Unknown function, General                        | -0.73 |
| GSU2885 |      | NHL repeat domain protein                                   | Unknown function, General                        | -0.77 |
| GSU1394 |      | laccase family protein                                      | Unknown function, General                        | -0.86 |
| GSU1048 |      | SEC-C motif domain protein                                  | Unknown function, General                        | -0.87 |
| GSU1741 |      | phosphatase, Ppx/GppA family                                | Unknown function, Enzymes of unknown specificity | -0.89 |
| GSU2571 |      | Rrf2 family protein   | Unknown function, General                        | -0.92 |
| GSU1596 |      | Sua5/YciO/YrdC/YwlC family protein                          | Unknown function, General                        | -0.98 |



|         |  |  |  |       |
|---------|--|--|--|-------|
| GSU1798 |  | 2-isopropylmalate synthase/homocitrate synthase family protein | Unknown function, General                        | -1.02 |
| GSU3280 |  | thioredoxin-related protein                                    | Unknown function, General                        | -1.06 |
| GSU1338 |  | heavy-metal-associated domain protein                          | Unknown function, General                        | -1.08 |
| GSU1210 |  | metallo-beta-lactamase family protein                          | Unknown function, Enzymes of unknown specificity | -1.10 |
| GSU0825 |  | pirin family protein   | Unknown function, General                        | -1.13 |
| GSU1251 |  | BNR repeat domain protein                                      | Unknown function, General                        | -1.14 |
| GSU1477 |  | LemA family protein  | Unknown function, General                        | -1.16 |
| GSU1350 |  | thiF family protein  | Unknown function, General                        | -1.16 |
| GSU1904 |  | decarboxylase family protein                                   | Unknown function, Enzymes of unknown specificity | -1.17 |
| GSU0119 |  | glyoxalase family protein                                      | Unknown function, Enzymes of unknown specificity | -1.17 |
| GSU0237 |  | MaoC-like domain protein                                       | Unknown function, General                        | -1.19 |
| GSU2436 |  | dehydrogenase complex, E1 component, beta subunit              | Unknown function, Enzymes of unknown specificity | -1.24 |
| GSU0117 |  | aminotransferase, classes I and II                             | Unknown function,                                | -1.24 |

|         |      |                                     |   |       |
|---------|------|-------------------------------------|---|-------|
|         |      |                                     | Enzymes of unknown specificity                      |       |
| GSU1166 |      | TPR domain protein                  | Unknown function,<br>General                        | -1.26 |
| GSU1945 |      | fibronectin type III domain protein | Unknown function,<br>General                        | -1.26 |
| GSU2296 |      | HD domain protein                   | Unknown function,<br>General                        | -1.27 |
| GSU0448 |      | hydrolase, putative                 | Unknown function,<br>Enzymes of unknown specificity | -1.28 |
| GSU2063 |      | HD domain protein                   | Unknown function,<br>General                        | -1.30 |
| GSU0360 |      | OmpA domain protein                 | Unknown function,<br>General                        | -1.35 |
| GSU2977 |      | transaldolase, putative             | Unknown function,<br>Enzymes of unknown specificity | -1.39 |
| GSU1266 | lepA | GTP-binding protein LepA            | Unknown function,<br>General                        | -1.41 |
| GSU0853 |      | CBS domain protein                  | Unknown function,<br>General                        | -1.41 |
| GSU0685 |      | radical SAM domain protein          | Unknown function,<br>Enzymes of unknown specificity | -1.42 |
| GSU2442 |      | RelA/SpoT domain protein            | Unknown function,<br>General                        | -1.44 |
| GSU1442 |      | carbonic anhydrase family protein   | Unknown function,<br>Enzymes of unknown specificity | -1.44 |

|         |        |   |  |       |
|---------|--------|---|--|-------|
| GSU2263 |        | oxidoreductase, Gfo/Idh/MocA family                           | Unknown function, Enzymes of unknown specificity | -1.47 |
| GSU0810 |        | OmpA domain protein   | Unknown function, General                        | -1.50 |
| GSU3062 |        | radical SAM domain iron-sulfur cluster-binding oxidoreductase | Unknown function, Enzymes of unknown specificity | -1.50 |
| GSU1701 |        | diadenosine polyphosphate hydrolase, FHIT domain-containing   | Unknown function, General                        | -1.51 |
| GSU3059 |        | radical SAM domain iron-sulfur cluster-binding oxidoreductase | Unknown function, Enzymes of unknown specificity | -1.57 |
| GSU1839 |        | phosphatase/phosphohexomutase-related hydrolase               | Unknown function, Enzymes of unknown specificity | -1.57 |
| GSU0023 |        | TPR domain protein  | Unknown function, General                        | -1.58 |
| GSU1345 |        | transcriptional regulator, Rrf2 family                        | Unknown function, General                        | -1.58 |
| GSU1496 | pilA   | geopilin  | Unknown function, General                        | -1.58 |
| GSU0442 | mqnC-1 | dehypoxanthinylfualosine cyclase, putative                    | Unknown function, Enzymes of unknown specificity | -1.60 |
| GSU3092 | yqeY   | uncharacterized protein YqeY                                  | Unknown function, General                        | -1.62 |
| GSU1868 |        | cysteine desulfurase family protein                           | Unknown function, Enzymes of unknown specificity | -1.62 |

|         |        |  |  |       |
|---------|--------|--|--|-------|
| GSU1866 |        | PhoH-related ATPase  | Unknown function,<br>General                           | -1.65 |
| GSU2183 |        | Fic family protein   | Unknown function,<br>General                           | -1.65 |
| GSU2074 |        | peptidylprolyl cis-trans isomerase,<br>PpiC-type                                     | Unknown function,<br>General                           | -1.65 |
| GSU1002 |        | YcaC-related hydrolase, putative   | Unknown function,<br>Enzymes of unknown<br>specificity | -1.66 |
| GSU0654 | thiF-1 | thiamin biosynthesis<br>thiocarboxylate synthase                                     | Unknown function,<br>General                           | -1.66 |
| GSU2285 |        | membrane-associated metal-<br>dependent phosphohydrolase, HDc<br>domain-containing   | Unknown function,<br>General                           | -1.70 |
| GSU0542 |        | diguanylate cyclase  | Unknown function,<br>General                           | -1.73 |
| GSU3213 | obgE   | ribosome biogenesis GTPase<br>ObgE   | Unknown function,<br>General                           | -1.74 |
| GSU2435 | aceF   | pyruvate dehydrogenase complex,<br>E2 protein, dihydrolipoamide<br>acetyltransferase | Unknown function,<br>Enzymes of unknown<br>specificity | -1.74 |
| GSU3376 |        | response receiver-modulated<br>diguanylate cyclase                                   | Unknown function,<br>General                           | -1.77 |
| GSU1802 | yjeF   | YjeF-related putative carbohydrate<br>kinase   | Unknown function,<br>General                           | -1.78 |
| GSU3013 | engB   | GTPase EngB  | Unknown function,<br>General                           | -1.79 |
| GSU1844 |        | IPT/TIG domain protein, putative   | Unknown function,<br>General                           | -1.79 |

Table B15:  $\Delta z$ -score of proteins involved in protein biosynthesis.  $\Delta z$ -score was calculated as follows: (z-score in U treatment - z-score in control)

| Locus ID | Symbol | Name   | Category  | $\Delta z$ |
|----------|--------|--|---|------------|
| GSU3373  | rsmB   | 16S rRNA (5-methyl-C967)-methyltransferase                                     | Protein synthesis, tRNA and rRNA base modification                | 1.73       |
| GSU3464  | gidA   | tRNA (5-carboxymethylaminomethyl-2-thio-U34)-formylglycyltransferase/reductase | Protein synthesis, tRNA and rRNA base modification                | 1.71       |
| GSU2569  | mnmA   | tRNA (5-carboxymethylaminomethyl-2-thio-U34)-thioltransferase                  | Protein synthesis, tRNA and rRNA base modification                | 1.66       |
| GSU0648  | rplS   | ribosomal protein L19  | Protein synthesis, Ribosomal proteins: synthesis and modification | 1.62       |
| GSU2850  | rplP   | ribosomal protein L16  | Protein synthesis, Ribosomal proteins: synthesis and modification | 1.62       |
| GSU1463  | aspS   | aspartyl-tRNA synthetase   | Protein synthesis, tRNA aminoacylation                            | 1.58       |
| GSU2045  | valS   | valyl-tRNA synthetase  | Protein synthesis, tRNA aminoacylation                            | 1.56       |
| GSU2838  | rplO   | ribosomal protein L15  | Protein synthesis, Ribosomal proteins: synthesis and modification | 1.52       |
| GSU1810  | tilS   | tRNA(Ile)-lysine synthetase  | Protein synthesis, tRNA and rRNA base modification                | 1.51       |

|         |        |   |   |      |
|---------|--------|---|---|------|
| GSU2875 | rpsI   | ribosomal protein S9                              | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | 1.50 |
| GSU2232 | metG   | methionyl-tRNA synthetase                         | Protein synthesis, tRNA<br>aminoacylation                               | 1.46 |
| GSU3366 | glnS   | glutaminyl-tRNA synthetase                        | Protein synthesis, tRNA<br>aminoacylation                               | 1.45 |
| GSU3467 | rpmH   | ribosomal protein L34                             | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | 1.42 |
| GSU3104 | prfA   | peptide chain release factor 1                    | Protein synthesis,<br>Translation factors                               | 1.40 |
| GSU1139 | tyrS   | tyrosyl-tRNA synthetase                           | Protein synthesis, tRNA<br>aminoacylation                               | 1.39 |
| GSU2844 | rpsN   | ribosomal protein S14                             | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | 1.38 |
| GSU1918 | frr    | ribosome recycling factor                         | Protein synthesis,<br>Translation factors                               | 1.37 |
| GSU2848 | rpsQ   | ribosomal protein S17                             | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | 1.36 |
| GSU2856 | rplD   | ribosomal protein L4                              | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | 1.35 |
| GSU2860 | fusA-3 | translation elongation factor G                   | Protein synthesis,<br>Translation factors                               | 1.31 |
| GSU3380 | gatB   | glutamyl-tRNA(Gln)<br>amidotransferase, B subunit | Protein synthesis, tRNA<br>aminoacylation                               | 1.25 |
| GSU1750 | infA   | translation initiation factor IF-1                | Protein synthesis,  | 1.22 |

|         |       |   |   |      |
|---------|-------|---|---|------|
|         |       |   | Translation factors   |      |
| GSU3136 | ileS  | isoleucyl-tRNA synthetase                               | Protein synthesis, tRNA aminoacylation                            | 1.11 |
| GSU1659 | hisS  | histidyl-tRNA synthetase                                | Protein synthesis, tRNA aminoacylation                            | 1.11 |
| GSU2209 | leuS  | leucyl-tRNA synthetase                                  | Protein synthesis, tRNA aminoacylation                            | 1.11 |
| GSU3379 |       | translation initiation factor, putative, aIF-2BI family | Protein synthesis, Translation factors                            | 0.94 |
| GSU2859 | tuf-1 | translation elongation factor Tu                        | Protein synthesis, Translation factors                            | 0.84 |
| GSU3381 | gatA  | glutamyl-tRNA(Gln) amidotransferase, A subunit          | Protein synthesis, tRNA aminoacylation                            | 0.83 |
| GSU1452 |       | RNA methyltransferase, TrmA family                      | Protein synthesis, tRNA and rRNA base modification                | 0.60 |
| GSU2839 | rpmD  | ribosomal protein L30                                   | Protein synthesis, Ribosomal proteins: synthesis and modification | 0.54 |
| GSU1709 | smpB  | SsrA-binding protein                                    | Protein synthesis, Other  | 0.47 |
| GSU2840 | rpsE  | ribosomal protein S5                                    | Protein synthesis, Ribosomal proteins: synthesis and modification | 0.38 |
| GSU2852 | rplV  | ribosomal protein L22                                   | Protein synthesis, Ribosomal proteins: synthesis and modification | 0.32 |
| GSU1219 | gltX  | glutamyl-tRNA synthetase                                | Protein synthesis, tRNA aminoacylation                            | 0.32 |
| GSU3465 | trmE  | tRNA modification GTPase TrmE                           | Protein synthesis, tRNA and rRNA base                             | 0.26 |

|         |      |                                      |   |       |
|---------|------|--------------------------------------|---|-------|
|         |      |                                      | modification  |       |
| GSU3205 |      | MiaB-like tRNA modifying enzyme YliG | Protein synthesis, tRNA and rRNA base modification                | 0.23  |
| GSU1592 | rpsO | ribosomal protein S15                | Protein synthesis, Ribosomal proteins: synthesis and modification | 0.21  |
| GSU1515 | thrS | threonyl-tRNA synthetase             | Protein synthesis, tRNA aminoacylation                            | 0.12  |
| GSU0662 | rplY | ribosoma protein L25                 | Protein synthesis, Ribosomal proteins: synthesis and modification | 0.05  |
| GSU0666 | rpsR | ribosomal protein S18                | Protein synthesis, Ribosomal proteins: synthesis and modification | 0.03  |
| GSU0130 | fmt  | methionyl-tRNA formyltransferase     | Protein synthesis, tRNA aminoacylation                            | 0.01  |
| GSU3307 |      | histidyl-tRNA synthetase, putative   | Protein synthesis, tRNA aminoacylation                            | 0.00  |
| GSU2271 | lysS | lysyl-tRNA synthetase                | Protein synthesis, tRNA aminoacylation                            | -0.02 |
| GSU1518 | rplT | ribosomal protein L20                | Protein synthesis, Ribosomal proteins: synthesis and modification | -0.07 |
| GSU0138 | prfC | peptide chain release factor 3       | Protein synthesis, Translation factors                            | -0.09 |
| GSU2847 | rplN | ribosomal protein L14                | Protein synthesis, Ribosomal proteins: synthesis and modification | -0.16 |
| GSU1460 | proS | prolyl-tRNA synthetase               | Protein synthesis, tRNA   | -0.26 |



|         |      |                                       |   |       |
|---------|------|---------------------------------------|---|-------|
|         |      |                                       | aminoacylation  |       |
| GSU2845 | rplE | ribosomal protein L5                  | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -0.28 |
| GSU2876 | rplM | ribosomal protein L13                 | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -0.39 |
| GSU1588 | infB | translation initiation factor IF-2    | Protein synthesis,<br>Translation factors                               | -0.41 |
| GSU2851 | rpsC | ribosomal protein S3                  | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -0.48 |
| GSU2234 | rpmB | ribosomal protein L28                 | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -0.49 |
| GSU0578 | glyQ | glycyl-tRNA synthetase, alpha subunit | Protein synthesis, tRNA aminoacylation                                  | -0.54 |
| GSU0668 | rplI | ribosomal protein L9                  | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -0.64 |
| GSU1517 | rpmI | ribosomal protein L35                 | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -0.65 |
| GSU1200 |      | ribosomal protein S1                  | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -0.67 |
| GSU2834 | rpsM | ribosomal protein S13                 | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -0.70 |
| GSU2830 | rplQ | ribosomal protein L17                 | Protein synthesis,<br>Ribosomal proteins:                               | -0.82 |

|         |        |   |   |       |
|---------|--------|---|---|-------|
|         |        |   | synthesis and modification  |       |
| GSU2843 | rpsH   | ribosomal protein S8                          | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -0.83 |
| GSU2865 | rplJ   | ribosomal protein L10                         | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -0.84 |
| GSU2866 | rplA   | ribosomal protein L1                          | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -0.89 |
| GSU3093 | rpsU-2 | ribosomal protein S21                         | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -0.89 |
| GSU1520 | pheT   | phenylalanyl-tRNA synthetase,<br>beta subunit | Protein synthesis, tRNA<br>aminoacylation                               | -0.90 |
| GSU1752 | efp-2  | translation elongation factor P               | Protein synthesis,<br>Translation factors                               | -0.90 |
| GSU2855 | rplW   | ribosomal protein L23                         | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -0.92 |
| GSU2871 | tuf-2  | translation elongation factor Tu              | Protein synthesis,<br>Translation factors                               | -0.96 |
| GSU0465 | efp-1  | translation elongation factor P               | Protein synthesis,<br>Translation factors                               | -0.99 |
| GSU1933 | fusA-1 | translation elongation factor G               | Protein synthesis,<br>Translation factors                               | -1.00 |
| GSU2858 | rpsJ   | ribosomal protein S10                         | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -1.02 |
| GSU0148 | alaS   | alanyl-tRNA synthetase                        | Protein synthesis, tRNA   | -1.03 |

|         |      |   |   |       |
|---------|------|---|---|-------|
|         |      |   | aminoacylation  |       |
| GSU2854 | rplB | ribosomal protein L2                    | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -1.03 |
| GSU1812 | argS | arginyl-tRNA synthetase                 | Protein synthesis, tRNA<br>aminoacylation                               | -1.09 |
| GSU1833 | trpS | tryptophanyl-tRNA synthetase            | Protein synthesis, tRNA<br>aminoacylation                               | -1.11 |
| GSU0579 | glyS | glycyl-tRNA synthetase, beta<br>subunit | Protein synthesis, tRNA<br>aminoacylation                               | -1.12 |
| GSU3235 | rpmA | ribosomal protein L27                   | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -1.18 |
| GSU3107 | rpmE | ribosomal protein L31                   | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -1.20 |
| GSU3365 | cysS | cysteinyl-tRNA synthetase               | Protein synthesis, tRNA<br>aminoacylation                               | -1.21 |
| GSU1599 | rpmF | ribosomal protein L32                   | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -1.24 |
| GSU2864 | rplL | ribosomal protein L7/L12                | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -1.27 |
| GSU2832 | rpsD | ribosomal protein S4                    | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -1.33 |
| GSU0037 | serS | seryl-tRNA synthetase                   | Protein synthesis, tRNA<br>aminoacylation                               | -1.35 |
| GSU2849 | rpmC | ribosomal protein L29                   | Protein synthesis,  | -1.37 |

|         |        |   |   |       |
|---------|--------|---|---|-------|
|         |        |   | Ribosomal proteins:<br>synthesis and modification                       |       |
| GSU3236 | rplU   | ribosomal protein L21                             | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -1.39 |
| GSU2867 | rplK   | ribosomal protein L11                             | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -1.40 |
| GSU2529 | fusA-2 | translation elongation factor G                   | Protein synthesis,<br>Translation factors                               | -1.41 |
| GSU1921 | rpsB   | ribosomal protein S2                              | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -1.43 |
| GSU0665 | rpsF   | ribosomal protein S6                              | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -1.44 |
| GSU3383 | gatC   | glutamyl-tRNA(Gln)<br>amidotransferase, C subunit | Protein synthesis, tRNA<br>aminoacylation                               | -1.45 |
| GSU2857 | rplC   | ribosomal protein L3                              | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -1.47 |
| GSU2861 | rpsG   | ribosomal protein S7                              | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -1.51 |
| GSU1516 | infC   | translation initiation factor IF-3                | Protein synthesis,<br>Translation factors                               | -1.51 |
| GSU2841 | rplR   | ribosomal protein L18                             | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -1.53 |
| GSU2206 | rpsT   | ribosomal protein S20                             | Protein synthesis,<br>Ribosomal proteins:                               | -1.54 |

|         |      |  |   |       |
|---------|------|--|---|-------|
|         |      |  | synthesis and modification  |       |
| GSU1886 | yfiA | ribosomal subunit associated sigma-54 modulation protein | Protein synthesis,<br>Translation factors                               | -1.55 |
| GSU2846 | rplX | ribosomal protein L24                                    | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -1.57 |
| GSU2853 | rpsS | ribosomal protein S19                                    | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -1.57 |
| GSU1519 | pheS | phenylalanyl-tRNA synthetase, alpha subunit              | Protein synthesis, tRNA aminoacylation                                  | -1.64 |
| GSU1920 | tsf  | translation elongation factor Ts                         | Protein synthesis,<br>Translation factors                               | -1.65 |
| GSU2603 | rpsA | ribosomal protein S1                                     | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -1.67 |
| GSU2842 | rplF | ribosomal protein L6                                     | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -1.69 |
| GSU0102 | selB | selenocysteine-specific translation elongation factor    | Protein synthesis,<br>Translation factors                               | -1.70 |
| GSU2833 | rpsK | ribosomal protein S11                                    | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -1.72 |
| GSU0643 | rpsP | ribosomal protein S16                                    | Protein synthesis,<br>Ribosomal proteins:<br>synthesis and modification | -1.73 |

Table B16:  $\Delta z$ -score of proteins with extrachromosomal element functions.  $\Delta z$ -score was calculated as follows: (z-score in U treatment - z-score in control)

| Locus ID | Symbol | Name                                      | Category  | Dz    |
|----------|--------|---|---|-------|
| GSU0053  |        | CRISPR-associated protein, GSU0053 family | Mobile and extrachromosomal element functions, Other                | 1.17  |
| GSU2280  |        | ISGsu7, transposase OrfA                  | Mobile and extrachromosomal element functions, Transposon functions | 0.60  |
| GSU1387  |        | CRISPR-associated protein, CT1975 family  | Mobile and extrachromosomal element functions, Other                | 0.50  |
| GSU0975  |        | phage tail sheath protein, putative       | Mobile and extrachromosomal element functions, Prophage functions   | -0.77 |

Table B17:  $\Delta z$ -score of proteins involved in transcription.  $\Delta z$ -score was calculated as follows: (z-score in U treatment - z-score in control)

| Locus ID | Symbol | Name                            | Category                          | $\Delta z$ |
|----------|--------|---------------------------------|-----------------------------------|------------|
| GSU1589  | rbfA   | ribosome-binding factor A       | Transcription, RNA processing     | 1.63       |
| GSU0189  | dbpA   | ATP-dependent RNA helicase DbpA | Transcription, Other              | 1.61       |
| GSU1485  |        | ribonuclease R, putative        | Transcription, Degradation of RNA | 1.22       |
| GSU3239  | cafA   | ribonuclease G                  | Transcription, RNA processing     | 1.07       |
| GSU2237  | rpoZ   | DNA-directed RNA polymerase,    | Transcription, DNA-               | 0.99       |

|         |        |  |   |       |
|---------|--------|--|---|-------|
|         |        | omega subunit                              | dependent RNA polymerase                    |       |
| GSU1887 | rpoN   | RNA polymerase sigma-54 factor             | Transcription, Transcription factors        | 0.97  |
| GSU1586 | nusA   | N utilization substance protein A          | Transcription, Transcription factors        | 0.76  |
| GSU3108 | rho    | transcription termination factor<br>Rho    | Transcription, Transcription factors        | 0.64  |
| GSU1795 | rph    | ribonuclease PH                            | Transcription, RNA processing               | 0.60  |
| GSU3089 | rpoD   | RNA polymerase sigma factor<br>RpoD        | Transcription, Transcription factors        | 0.58  |
| GSU2868 | nusG   | transcription antitermination protein NusG | Transcription, Transcription factors        | 0.52  |
| GSU2831 | rpoA   | DNA-directed RNA polymerase, alpha subunit | Transcription, DNA-dependent RNA polymerase | 0.51  |
| GSU1581 |        | polyA polymerase family protein            | Transcription, RNA processing               | 0.09  |
| GSU2235 |        | endoribonuclease L-PSP, putative           | Transcription, Degradation of RNA           | -0.19 |
| GSU1277 | greA   | transcription elongation factor<br>GreA    | Transcription, Transcription factors        | -0.43 |
| GSU1525 |        | RNA polymerase sigma-70 factor family      | Transcription, Transcription factors        | -0.55 |
| GSU0522 | rhIB   | ATP-dependent RNA helicase<br>RhIB         | Transcription, Degradation of RNA           | -0.60 |
| GSU0914 | rhIE-2 | ATP-dependent RNA helicase<br>RhIE         | Transcription, Other                        | -0.66 |
| GSU1593 | pnp    | polyribonucleotide                         | Transcription, Degradation                  | -0.91 |

|         |      |  |  |       |
|---------|------|--|--|-------|
|         |      | nucleotidyltransferase                           | of RNA   |       |
| GSU1692 | nusB | N utilization substance protein B                | Transcription,<br>Transcription factors            | -1.34 |
| GSU2863 | rpoB | DNA-directed RNA polymerase,<br>beta subunit     | Transcription, DNA-<br>dependent RNA<br>polymerase | -1.44 |
| GSU0921 |      | ribonuclease, Rne/Rng family<br>protein          | Transcription, RNA<br>processing                   | -1.57 |
| GSU0443 |      | ribonuclease D, putative                         | Transcription, RNA<br>processing                   | -1.66 |
| GSU2184 | ccaC | cytidine-specific tRNA<br>nucleotidyltransferase | Transcription, RNA<br>processing                   | -1.79 |

Table B18:  $\Delta z$ -score of proteins involved in fatty acid and phospholipid metabolism.  $\Delta z$ -score was calculated as follows: (z-score in U treatment - z-score in control)

| Locus ID | Symbol | Name   | Category   | $\Delta z$ |
|----------|--------|--|--|------------|
| GSU0242  | acpP-1 | acyl carrier protein   | Fatty acid and<br>phospholipid metabolism,<br>Biosynthesis | 1.71       |
| GSU2265  | fabZ   | (3R)-hydroxymyristoyl-(acyl-<br>carrier-protein) dehydratase | Fatty acid and<br>phospholipid metabolism,<br>Biosynthesis | 1.70       |
| GSU1103  |        | AMP-forming acyl-CoA<br>synthetase                           | Fatty acid and<br>phospholipid metabolism,<br>Degradation  | 1.66       |
| GSU0290  | fabH-1 | 3-oxoacyl-(acyl-carrier-protein)<br>synthase III             | Fatty acid and<br>phospholipid metabolism,<br>Biosynthesis | 1.65       |



|         |        |   |  |       |
|---------|--------|---|--|-------|
| GSU1402 | accA   | acetyl-CoA carboxylase, carboxyl transferase, alpha subunit | Fatty acid and phospholipid metabolism, Biosynthesis | 1.47  |
| GSU0688 | shc-1  | squalene-hopene cyclase                                     | Fatty acid and phospholipid metabolism, Other        | 1.42  |
| GSU1600 | plsX   | fatty acid/phospholipid synthesis protein PlsX              | Fatty acid and phospholipid metabolism, Biosynthesis | 1.21  |
| GSU1008 | fabI   | enoyl-(acyl-carrier-protein) reductase                      | Fatty acid and phospholipid metabolism, Biosynthesis | 0.93  |
| GSU1907 | pssA   | CDP-diacylglycerol--serine O-phosphatidyltransferase        | Fatty acid and phospholipid metabolism, Biosynthesis | 0.35  |
| GSU1603 | fabG-2 | 3-oxoacyl-(acyl-carrier-protein) reductase                  | Fatty acid and phospholipid metabolism, Biosynthesis | 0.33  |
| GSU1605 | fabF-2 | 3-oxoacyl-(acyl-carrier-protein) synthase II                | Fatty acid and phospholipid metabolism, Biosynthesis | -0.18 |
| GSU2020 | accB   | acetyl-CoA carboxylase, biotin carboxyl carrier protein     | Fatty acid and phospholipid metabolism, Biosynthesis | -0.37 |
| GSU0229 | alkK   | medium-chain-fatty-acid--CoA ligase                         | Fatty acid and phospholipid metabolism, Degradation  | -0.72 |
| GSU1601 | fabH-2 | 3-oxoacyl-(acyl-carrier-protein) synthase III               | Fatty acid and phospholipid metabolism, Biosynthesis | -0.73 |
| GSU3116 |        | 1-acyl-sn-glycerol-3-phosphate                              | Fatty acid and                                       | -0.76 |

|         |        |  |   |       |
|---------|--------|--|---|-------|
|         |        | acyltransferase, putative                                  | phospholipid metabolism,<br>Biosynthesis                |       |
| GSU2370 | accD   | acetyl-CoA carboxylase, carboxyl transferase, beta subunit | Fatty acid and phospholipid metabolism,<br>Biosynthesis | -0.91 |
| GSU0482 |        | cardiolipin synthetase, putative                           | Fatty acid and phospholipid metabolism,<br>Biosynthesis | -1.16 |
| GSU1604 | acpP-2 | acyl carrier protein                                       | Fatty acid and phospholipid metabolism,<br>Biosynthesis | -1.38 |
| GSU3313 |        | thiolase, putative   | Fatty acid and phospholipid metabolism,<br>Other        | -1.45 |
| GSU1602 | fabD   | malonyl CoA-acyl carrier protein transacylase              | Fatty acid and phospholipid metabolism,<br>Biosynthesis | -1.48 |
| GSU2019 | accC   | acetyl-CoA carboxylase, biotin carboxylase                 | Fatty acid and phospholipid metabolism,<br>Biosynthesis | -1.80 |

Table B19:  $\Delta z$ -score of proteins involved in DNA metabolism.  $\Delta z$ -score was calculated as follows: (z-score in U treatment - z-score in control)

| Locus ID | Symbol | Name   | Category   | $\Delta z$ |
|----------|--------|--|--|------------|
| GSU3470  | dnaA   | chromosomal replication initiator protein DnaA | DNA metabolism, DNA replication, recombination, and repair | 1.78       |
| GSU2549  | topA   | DNA topoisomerase I                            | DNA metabolism, DNA replication, recombination,            | 1.68       |

|         |       |  |  |      |
|---------|-------|--|--|------|
|         |       |  | and repair   |      |
| GSU3117 | ssb-2 | single-strand binding protein              | DNA metabolism, DNA replication, recombination, and repair | 1.67 |
| GSU1746 | ihfB  | integration host factor, beta subunit      | DNA metabolism, DNA replication, recombination, and repair | 1.47 |
| GSU1539 | xth   | exodeoxyribonuclease III                   | DNA metabolism, DNA replication, recombination, and repair | 1.45 |
| GSU0890 | ligA  | DNA ligase, NAD-dependent                  | DNA metabolism, DNA replication, recombination, and repair | 1.45 |
| GSU0541 | polA  | DNA polymerase I                           | DNA metabolism, DNA replication, recombination, and repair | 1.29 |
| GSU3090 | dnaG  | DNA primase                                | DNA metabolism, DNA replication, recombination, and repair | 1.17 |
| GSU2829 |       | deoxyribodipyrimidine photolyase, putative | DNA metabolism, DNA replication, recombination, and repair | 1.07 |
| GSU3371 |       | AP endonuclease, family 2                  | DNA metabolism, DNA replication, recombination, and repair | 0.77 |
| GSU0094 | dnaX  | DNA polymerase III, gamma and tau subunits | DNA metabolism, DNA replication, recombination, and repair | 0.73 |
| GSU2001 | mutL  | DNA mismatch repair protein MutL           | DNA metabolism, DNA replication, recombination, and repair | 0.39 |

|         |      |   |  |       |
|---------|------|---|--|-------|
| GSU0004 | gyrA | DNA gyrase, A subunit                   | DNA metabolism, DNA replication, recombination, and repair | 0.20  |
| GSU3266 |      | DNA helicase II, putative               | DNA metabolism, DNA replication, recombination, and repair | 0.05  |
| GSU0017 | mfd  | transcription-repair coupling factor    | DNA metabolism, DNA replication, recombination, and repair | -0.14 |
| GSU1822 |      | DNA mismatch repair protein MutS        | DNA metabolism, DNA replication, recombination, and repair | -0.26 |
| GSU1766 | xseB | exodeoxyribonuclease VII, small subunit | DNA metabolism, Degradation of DNA                         | -0.43 |
| GSU0001 | dnaN | DNA polymerase III, beta subunit        | DNA metabolism, DNA replication, recombination, and repair | -0.43 |
| GSU2230 | holB | DNA polymerase III, delta prime subunit | DNA metabolism, DNA replication, recombination, and repair | -0.58 |
| GSU1401 | dnaE | DNA polymerase III, alpha subunit       | DNA metabolism, DNA replication, recombination, and repair | -0.87 |
| GSU1326 | recG | ATP-dependent DNA helicase RecG         | DNA metabolism, DNA replication, recombination, and repair | -1.01 |
| GSU0003 | gyrB | DNA gyrase, B subunit                   | DNA metabolism, DNA replication, recombination             | -1.05 |
| GSU2064 | recN | DNA repair protein RecN                 | DNA metabolism, DNA replication, recombination             | -1.06 |
| GSU0143 |      | competence/damage-inducible             | DNA metabolism, DNA  | -1.09 |

|         |        |  |  |       |
|---------|--------|--|--|-------|
|         |        | protein CinA   | replication, recombination,<br>and repair                        |       |
| GSU1044 |        | mutT/nudix family protein                            | DNA metabolism, DNA<br>replication, recombination,<br>and repair | -1.38 |
| GSU1076 | ruvA   | Holliday junction DNA helicase<br>RuvA               | DNA metabolism, DNA<br>replication, recombination,<br>and repair | -1.41 |
| GSU1725 | sbcC-2 | DNA repair exonuclease SbcCD,<br>C subunit, putative | DNA metabolism, DNA<br>replication, recombination,<br>and repair | -1.51 |
| GSU0547 | mutS-2 | DNA mismatch repair ATPase<br>MutS-2                 | DNA metabolism, Other  | -1.52 |
| GSU1521 | ihfA-1 | integration host factor, alpha<br>subunit            | DNA metabolism, DNA<br>replication, recombination,<br>and repair | -1.53 |
| GSU2207 | hola   | DNA polymerase III, delta subunit                    | DNA metabolism, DNA<br>replication, recombination,<br>and repair | -1.59 |
| GSU2602 | ihfB-2 | DNA-binding protein HU                               | DNA metabolism,<br>Chromosome-associated<br>proteins             | -1.60 |
| GSU0145 | recA   | recA protein   | DNA metabolism, DNA<br>replication, recombination,<br>and repair | -1.60 |
| GSU3132 | hup    | histone-like protein                                 | DNA metabolism,<br>Chromosome-associated<br>proteins             | -1.64 |
| GSU1199 |        | nuclease, putative                                   | DNA metabolism,<br>Degradation of DNA                            | -1.74 |

## APPENDIX C

### SUPPLEMENTARY INFORMATION NOVEL MEMBRANE-BOUND COMPLEXES INVOLVED IN ENERGY CONSERVATION BY THE ACETATE OXIDIZING SULFATE-REDUCING BACTERIUM *DESULFOBACTER* *POSTGATEI*

#### Genome sequence the sulfate reducing bacteria *Desulfobacter postgatei*

##### General Features of the *D. postgatei* Genome

Together with *Desulfobacter curvatus* (<http://www.ncbi.nlm.nih.gov/bioproject/?term=169816>), the one of *D. postgatei* is the second acetate-oxidizing, sulfate-reducing bacteria whose genome sequence has been completely sequenced. The genome of *D. postgatei* 2ac9 consist of a single, circular chromosome of 3,974,658 base pairs (bp) (Accession NZ\_CM001488 NZ\_AGJR02000000). The automated annotation process identified 3,773 genes predicted, 3,678 were proteins coding genes, 95 RNAs, and 238 were predicted as pseudogenes (Table C1). The majority of the intact protein-coding genes (2,742) were assigned with a putative function while the remaining ones (936) were annotated as hypothetical proteins.

Table C1: Genome statistics of *Desulfobacter postgatei*

| Attribute                       | Value     | % of total |
|---------------------------------|-----------|------------|
| Genome size (bp)                | 3,974,658 | 100.00%    |
| DNA coding number of bases (bp) | 3,419,080 | 86.02%     |
| DNA G+C number of bases         | 1,874,851 | 47.17%     |
| Extrachromosomal elements       | 0         |            |
| Genes total number              | 3,773     | 100.00%    |
| Protein coding genes            | 3,678     | 97.48%     |
| RNA genes                       | 95        | 2.52%      |
| Pseudo genes                    | 238       | 6.31%      |

|  |       |        |
|--|-------|--------|
| Protein coding genes with function prediction    | 2,742 | 72.67% |
| Protein coding genes without function prediction | 936   | 24.81% |

### **Energy metabolism**

*D. postgatei* grows heterotrophically using acetate as electron donor for sulfate reduction as sole energy source (241). Therefore, they thrive in habitats where acetate and sulfate are permanently available (242). Although many components of its central metabolism were already described by biochemical experiments, the genome sequence and subsequent results obtained by this study revealed novel features that are relevant for energy metabolism, including the H<sup>+</sup>-translocating ferredoxin:NAD<sup>+</sup> oxidoreductase (Rnf complex), Quinone-interacting oxidoreductase (Qmo complex), NADH-dependent reduced ferredoxin:NADP<sup>+</sup> oxidoreductase (Nfn complex), Ech-hydrogenase-related complex (Ehr complex), and Quinone reductase (Qrc complex). Relevant features of the carbon and energy metabolism of *D.postgatei* are explained in the following sections.

### **Acetate uptake**

Mainly, acetate enters the cell by active transportation across the cell membrane using the proton or sodium gradient (243). In environments where acetate concentration is low, acetate uptake likely proceeds via active transport. In contrast, in environments in which acetate is available in high concentration, this likely enters to the cell through passive form, associates with a proton in the periplasm and diffuses through the membrane as acetic acid (243).

### **Sulfate uptake**

Since sulfate reduction takes place in the cytoplasm and the membrane of *D. postgatei* is not permeable to sulfate ions, sulfate has to be transported into the cell by an active specific transporter (242). The genome annotation suggested there are different types of uptake system for sulfate in *D. postgatei* depending upon the environmental conditions. For instance, in environments where sulfate concentrations are low, such as freshwater, sulfate uptake might be performed via the high-affinity proton-driven

symporters, SulP (DespoDRAFT\_02318), and the ABC-type transport system, cysATP (DespoDRAFT\_01411). In environments where sulfate concentrations are often high, such as brackish and marine mud, uptake of sulfate is likely to be driven by an energy-independent sodium translocation (244).

### **Citric Acid Cycle**

Initial characterization of the central metabolism of *D.postgatei* has revealed that all enzymes for a citric acid cycle were found (245). However, further experiments have shown an unusual utilization of a reductive citric acid cycle in reverse, similar to those observed in green sulfur bacteria (245-247) that allow the net production of 1 ATP via substrate phosphorylation (248). Briefly, the citric acid cycle in *D.postgatei* can be explained in the following steps.

Initially, acetate is activated via succinyl-CoA:acetate CoA transferase (DespoDRAFT\_02073) to acetyl-CoA and succinate. The acetyl-CoA is taken by the reversible ATP citrate lyase generating citrate and one additional mol of ATP by substrate level phosphorylation (153). The DespoDRAFT\_02935 and DespoDRAFT\_02936 are contiguous genes encoding the alpha and beta subunits of ATP citrate lyase, respectively. This step is a peculiarity of *D.postgatei* metabolism because the formation of citrate is catalyzed rather by citrate synthase in many other acetate-oxidizing bacteria and ATP citrate lyase was hypothesized to be restricted to only autotrophic bacteria (246, 249).

Genes for aconitate hydratase (DespoDRAFT\_00706), a NADP-dependent isocitrate dehydrogenase (DespoDRAFT\_00291) and the four subunits of 2-oxoglutarate ferredoxin oxidoreductase (DespoDRAFT\_00203 - DespoDRAFT\_00206) were also found in the genome as they were previously described *D.postgatei* (246). The 2-oxoglutarate ferredoxin oxidoreductase catalyzes the reversible decarboxylation of 2-oxoglutarate to form succinyl-CoA. As another peculiarity of the *D.postgatei* metabolism, this step is mediated by ferredoxin, instead of NAD, as many other anaerobes (250). Genes for the three subunits of the membrane bound succinate dehydrogenase (DespoDRAFT\_02909 - DespoDRAFT\_02911) were found located contiguously in the genome. Because succinate oxidation is coupled to the reduction of



quinones in an endergonic reaction, succinate dehydrogenase contains a *b*-type cytochrome subunit traversing the membrane capable of reversibly transferring electrons to quinone and use the proton gradient as a source of energy (229). The reversible hydration of fumarate is carried out by a cytoplasmic fumarate hydratase (DespoDRAFT\_00633) and the oxidation of malate is catalyzed by a membrane-bound malate dehydrogenase (DespoDRAFT\_00212). Previous biochemical studies suggested that malate oxidation could not be coupled to the reduction of NAD or NADP and due to the limited redox potential, this reaction could not also be coupled to proton translocation (246). Therefore, we hypothesized that DsrC, a cytoplasmic disulfide enzyme that interacts directly with the dissimilatory sulfite reductase, couples the direct oxidation of malate to the reduction of sulfite (163). In synthesis, the citric acid cycle in *D. postgatei* yields one reduced NADPH, one reduced ferredoxin, one reduced quinone, and one electron utilized in the reduction of DsrC in addition to the 1 mol of ATP produced by the ATP citrate lyase (Figure C1).

### **Anapleurotic reactions**

Anapleurotic pathway is a set of important reactions that connect, bypass and replenish citric acid cycle intermediates that have been utilized as building blocks for anabolic purposes (251). Labeling and physiological studies have previously shown that *D. postgatei* contains the same anapleurotic sequence for the citric acid cycle found in *Desulfuromonas acetoxidans*. This pathway goes from acetate to phosphoenolpyruvate (acetate → acetyl-P → acetyl-CoA → pyruvate → phosphoenolpyruvate) (Figure C1)(248).

Genes encoding the key enzymes for this set of reactions were found in the genome of *D. postgatei* (Figure C1). The phosphorylation of acetate is catalyzed by acetate kinase, *ackr*, and the conversion of acetyl-P to acetyl-CoA by phosphate transacetylase, *pta*. Two further pathways for the activation of acetate, the ADP-forming acetate-CoA ligase, *acs1*, and the AMP-forming acetate-CoA ligase, *acs2*, were identified. The conversion of acetyl-CoA into pyruvate is catalyzed by pyruvate ferredoxin oxidoreductase, *por*. The phosphorylation of pyruvate to phosphoenolpyruvate can be carried out by three different enzymes. Genes encoding for the enzymes pyruvate

kinase, pyruvate phosphate dikinase, and phosphoenolpyruvate synthase were also identified. Pyruvate carboxylase and phosphoenolpyruvate carboxylase appear to be the main connection between this set of reactions and the citric acid cycle (Figure C1).

As in the Fe(III)-reducing bacteria, *Geobacter sulfurreducens*, anapleurotic reactions have two distinguishable features. They can alternate pathways and provide metabolic redundancy that enables *D.postgatei* to resist potential events of genetic perturbation which is essential to maintain the robustness of its specialist metabolism (252-254). We hypothesized that the anapleurotic reactions can also be utilized as futile cycles to counteract the overproduction of ATP under certain conditions, allowing bacteria to regulate catabolic and anabolic functions.

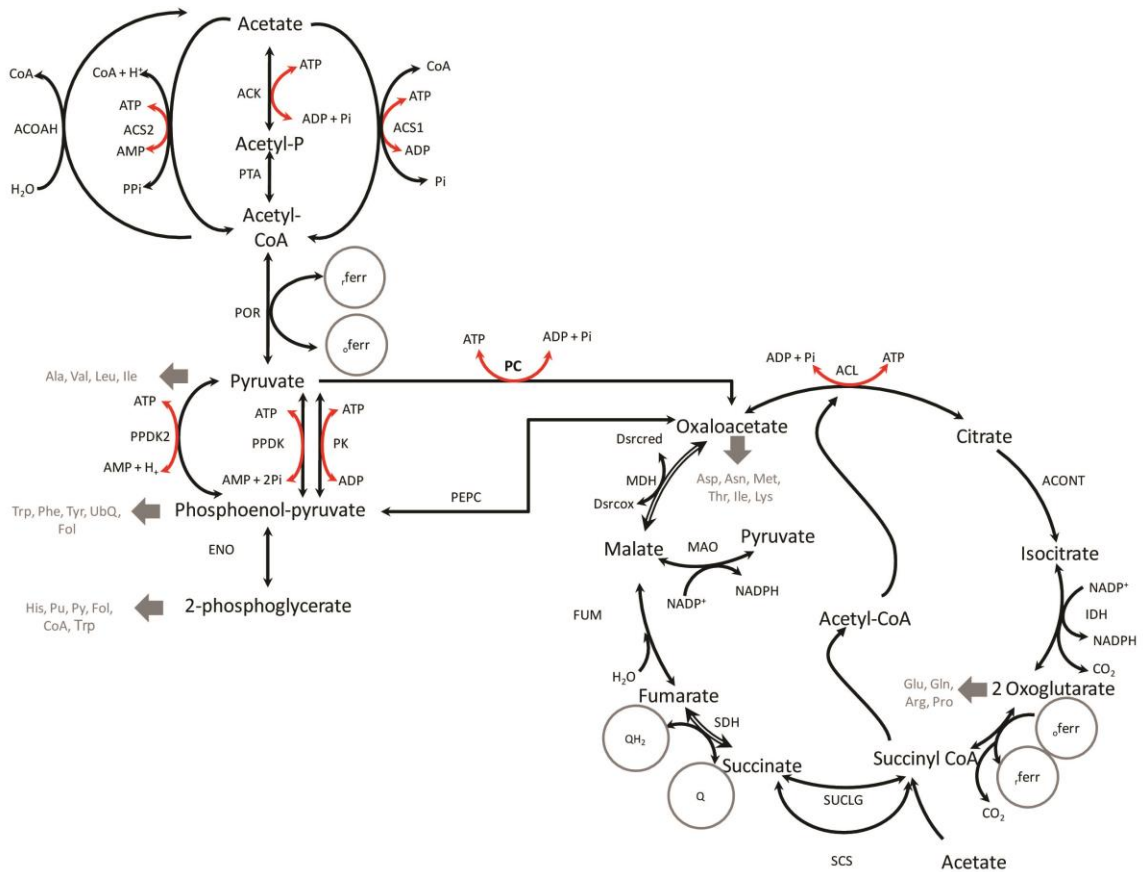


Figure C1: Anapleurotic reactions and the citric acid cycle of *D.postgatei*. Arrows directions indicate the reversibility of the reactions. Striped arrows indicate that the

reaction is predicted to be catalyzed by a membrane-bound enzyme. Red arrows indicate reactions that produce or consume ATP. In circles are the reducing equivalents, QH<sub>2</sub>: reduced quinone, Q: oxidized quinone, <sub>r</sub>ferr: reduced ferredoxin, and <sub>o</sub>ferr: oxidized ferredoxin. The abbreviations indicate the name of each reaction. Abbreviations and the locus name of the genes encoding these enzymes are the following: ACK, Acetate kinase (DespoDRAFT\_00806); PTA, Phosphotransacetylase (DespoDRAFT\_00751); ACS1, Acetate-CoA ligase (ADP-forming) (DespoDRAFT\_00221); ACS2, Acetate-CoA ligase (AMP-forming) (DespoDRAFT\_00810); ACOAH, Acetyl-CoA hydrolase (DespoDRAFT\_00482); POR, Pyruvate ferredoxin oxidoreductase (DespoDRAFT\_02687, DespoDRAFT\_02688, and DespoDRAFT\_00515); PK, Pyruvate kinase (DespoDRAFT\_02186); PPK, Pyruvate phosphate dikinase (DespoDRAFT\_02139); PPK2, Phosphoenolpyruvate synthase (DespoDRAFT\_00514); PC, Pyruvate carboxylase (DespoDRAFT\_00286 and DespoDRAFT\_01944); PEPC, Phosphoenolpyruvate carboxylase (DespoDRAFT\_00104); ENO, Enolase (DespoDRAFT\_03029); SUCLG, Succinyl:acetate CoA transferase (DespoDRAFT\_02073); SCS, Succinyl-CoA synthetase (DespoDRAFT\_02935 and DespoDRAFT\_02936); ACL, ATP-dependent citrate lyase (DespoDRAFT\_00153 and DespoDRAFT\_00154); ACONT, Aconitase (DespoDRAFT\_00181 and DespoDRAFT\_00706); IDH, Isocitrate dehydrogenase (DespoDRAFT\_00291); KGOR, 2-oxoglutarate ferredoxin oxidoreductase (DespoDRAFT\_00203, DespoDRAFT\_00204, DespoDRAFT\_00205, and DespoDRAFT\_00206); SDH, Succinate dehydrogenase (DespoDRAFT\_02909, DespoDRAFT\_02910, and DespoDRAFT\_02911); FUM, Fumarate hydratase (DespoDRAFT\_00633); MDH, Malate dehydrogenase (DespoDRAFT\_00292) and MAO, Malate oxidoreductase (DespoDRAFT\_02908). Biomass building blocks are indicated in gray. The abbreviations are the following: Trp, Tryptophan; Phe, Phenylalanine; Tyr, Tyrosine; UbQ, Ubiquinone; Fol, Folate; Pu, Purines; Py, Pyrimidines; CoA, Coenzyme A; Asp, Aspartate; Asn, Asparagine; Met, Methionine; Thr, Threonine; Ile, Isoleucine; Lys, Lysine; Glu, Glutamate; Gln, Glutamine; Arg, Arginine; Pro, Proline; Ala, Alanine; Val, Valine and Leu, Leucine.

## Sulfate reduction

*D. postgatei* can utilize sulfate, sulfite, and thiosulfate as electron acceptors to produce hydrogen sulfide (242). The pathway of sulfate reduction involves the same set of reactions than other SBR previously characterized (250). Briefly, once sulfate enters the cell, it is activated via sulfate adenylyltransferase, *sat*, to form adenosine 5'-phosphosulfate (APS). In the following step, APS is reduced to sulfite by adenosine 5-phosphosulfate reductase, *aprA* and *aprB*. The final step of sulfate reduction, sulfite reduction, is carried out by dissimilatory sulfite reductase, *dsrA* and *dsrB*. Since one of the remaining question in the metabolism of *D.postgatei* correspond to the nature of electron donors utilized by these enzymes, we focused our analysis on the complexes that have been recently described in other SBR and have been found for the first time in *D. postgatei*.

## QmoABC complex

From a thermodynamic point of view, sulfate reduction is not an easy task. The redox potential of the sulfate/sulfite couple is extremely low (-516 mV) making sulfate very unwilling to accept electrons (255). Therefore, *D.postgatei* has to spend 2 moles of ATP to produce adenosine phosphosulfate (APS) from sulfate to allow its reduction by intracellular electron mediators, such as ferredoxin or NADH (-398 mV and -314 mV, respectively) (199). As mentioned before, the activation of sulfate is catalyzed by a sulfate adenylyltransferase, encoded by DespoDRAFT\_02886 (*sat*). In the following step, APS is reduced to sulfite by adenosine 5-phosphosulfate reductase, encoded by DespoDRAFT\_00746 (*aprA*) and DespoDRAFT\_00747 (*aprB*)(163).

Previous studies in the sulfate-reducing bacteria *Desulfovibrio desulfuricans* have shown that electrons utilized by APS reductase derive from QmoABC, a recently described complex that is essential for sulfate reduction (256, 257). This complex mediates the electron transfer from the reduced quinone pools to the reduction of APS (Figure 4)(256, 258).

Genes encoding the three subunits of this complex were found in the genome of *D.postgatei* contiguously to adenosine phosphosulfate reductase, *aprA*, as in other SRBs

(163). Further experiments in *D.desulfuricans* showed that QmoABC (for Quinone-interacting membrane-bound oxidoreductase) complex and the APS reductase interacts directly, however they failed to detect electron transfer between only the two enzymes, suggesting that bifurcation or confurcation mechanism could be involved (256). This has been supported by the fact that membrane potential cannot drive electron transfer from the periplasm-facing transmembrane, QmoC, to the cytoplasmic AprAB, and a more energetically favorable reaction, such as ferredoxin oxidation, must be utilized (256). The transmembrane member of the QmoABC complex, the cytochrome *b* containing QmoC, is the hypothesized responsible to couple this reaction to chemiosmotic energy conservation (161). The role of QmoABC in energy conservation and sulfate reduction and its interactions with other enzymes deserves further consideration.

### **DsrMKJOP complex**

A second membrane-bound complex, DsrMKJOP, transfers the electrons derived from oxidation of electron donor to sulfite, the product resulting from APS reduction. Likewise QmoABC, the DsrMKJOP complex is also involved in generation of proton motive force (259). This transmembrane complex is composed by five subunit DsrP, DsrO, DsrJ, DsrK, and DsrM and its function is to couple the oxidation of quinones to the reduction of the cytoplasmic electron carrier, DsrC, that further delivers two electrons to the dissimilatory sulfite reductase enzyme, DsrAB (155, 157) (Figure 4).

Genes encoding the two subunits of the dissimilatory sulfite reductase A and B, DespoDRAFT\_01364, and DespoDRAFT\_01365, were found to be located contiguously as in other sulfate SRB (Figure C2) (211, 260-263). With few exceptions, both DsrMKJOP and QmoABC complexes are conserved in the genomes of sulfate-reducing bacteria described so far. In those microorganisms that lack these complexes, a simpler version of them is present (261).

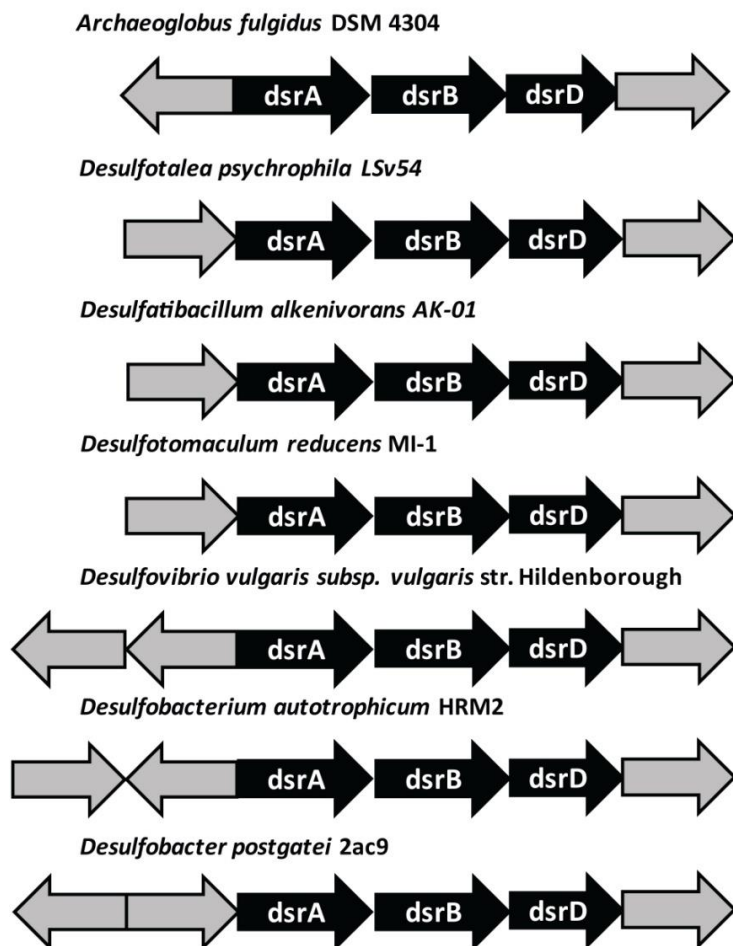


Figure C2: Genomic context of the *dsr* genes of *D.postgatei* and comparison with other SRB.

### **Nfn (NADH-dependent reduced ferredoxin:NADP<sup>+</sup> oxidoreductase) complex**

Reverse electron bifurcation, also known as electron confurcation, has been proposed as a mechanism that allows that the endergonic reduction of APS by reduced quinone is coupled to its exergonic reduction by a low-potential soluble electron donor, such as ferredoxin (255). This mechanism aims to increase the yield of reduced ferredoxin, which can be further used by Rnf complex to pump additional ions into the periplasm towards to energy conservation (240, 264).

Electron confurcation by Nfn complex was formerly described in *Clostridium kluuyveri* (264), and homologs for the two subunits have been found in the genomes of *D. vulgaris* Hildenborough and *D. alaskensis* G20 (240). Genes encoding the two subunits

of the soluble NADH-dependent reduced ferredoxin:NADP<sup>+</sup> oxidoreductase A (DespoDRAFT\_02087) and B (DespoDRAFT\_02088) were found to be located contiguously in the genome of *D. postgatei*. Since *D.postgatei* central metabolism contains a NADPH<sup>+</sup>-dependent isocitrate dehydrogenase (DespoDRAFT\_00291, Figure C1), we predict Nfn complex provides a link between two moles of NADPH<sup>+</sup> toward to the reduction of one ferredoxin and one NAD.

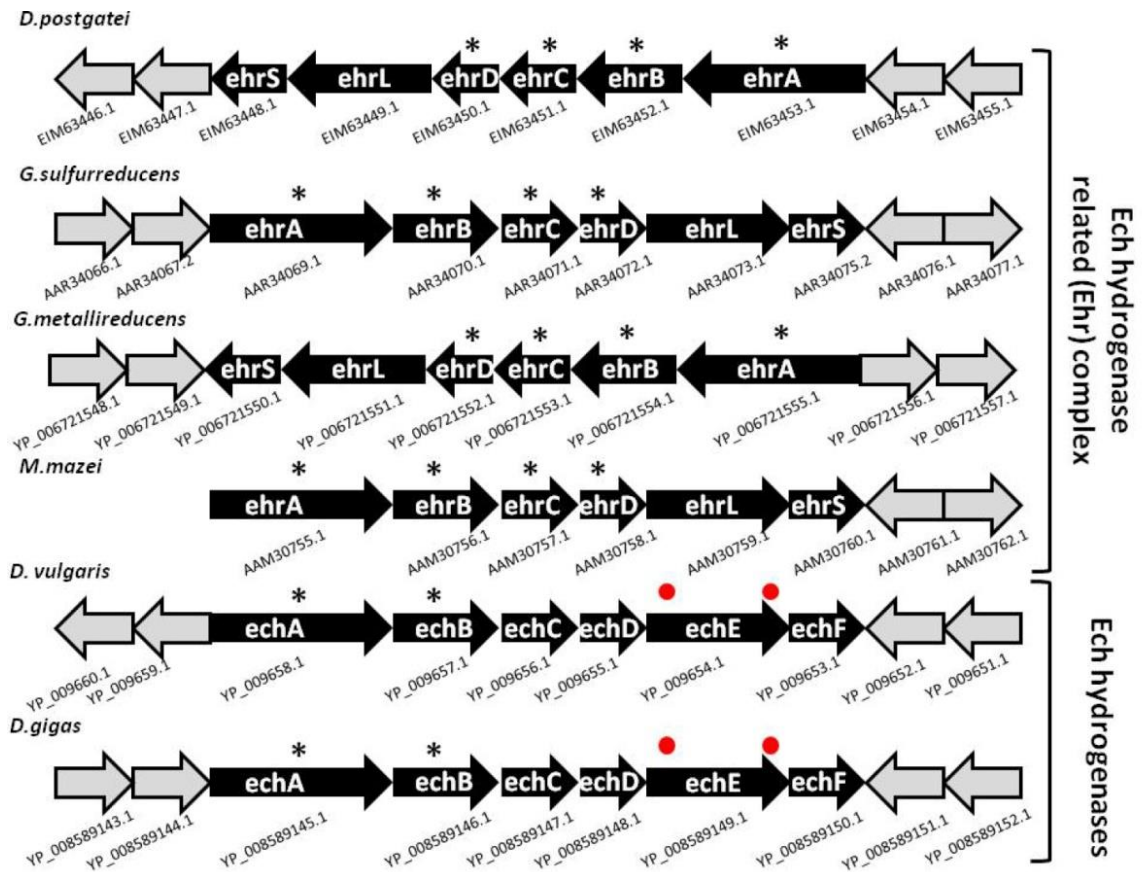


Figure C3: Comparison of the Ech hydrogenases in *D.vulgaris* and *D.gigas* with the Ech-hydrogenase-related (Ehr) complex present in *D.postgatei*, *G.sulfurreducens*, *G.metallireducens*, and *M.mazei*. The subunits encoding Ech hydrogenases and Ech-hydrogenase-related are in black. Asterisk marks indicate the trans-membrane helix(ces) predicted by TMHMM Server v. 2.0 (239). Red circles indicate CxxC motifs containing the cysteine residues in the N- and C-termini.







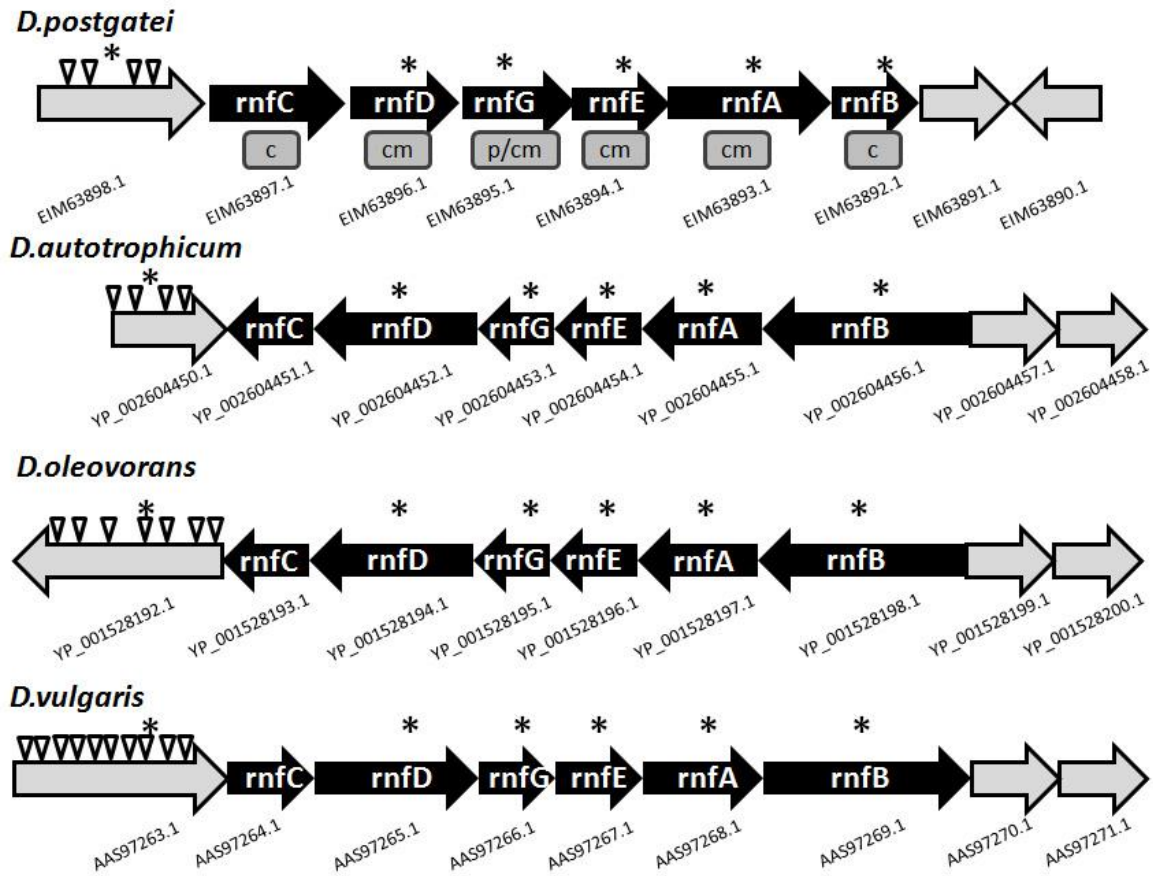


Figure C5: Comparison of the *D. postgatei* *rnf* cluster (DespoDRAFT\_01992 - DespoDRAFT\_01997) to those of *D. autotrophicum* (211), *D. oleovorans* (163), and *D. vulgaris* (268). The subunits encoding for the H<sup>+</sup>-translocating ferredoxin:NAD<sup>+</sup> oxidoreductase (Rnf complex) are in black. Gray boxes below *D. postgatei* *rnf* cluster show the localization of each subunit predicted by PSORTB (269); c stands for Cytoplasmic, cm stands for Cytoplasmic Membrane, and p for Periplasmic. Asterisk marks indicate the trans-membrane helix(es) predicted by TMHMM Server v. 2.0 (239). Triangles indicate the CXXCH motif for the *c*-type cytochrome found besides the *rnf* cluster.

### Response to environmental challenges

The genome of *D. postgatei* revealed its potential to respond to a variety of environmental stimuli. We found 40 putative genes coding for sensor histidine kinase, and 22 chemotaxis related genes. *In contrast* with previous observations, *D. postgatei*

seems to be motile by flagella under conditions where nutrients were nearly depleted (Figure C18 and Figure C20) (242). The genes for flagella biosynthesis are mainly arranged in the two clusters, DespoDRAFT\_00538-DespoDRAFT\_00610 and DespoDRAFT\_02845-DespoDRAFT\_02854, and chemotaxis genes are located adjacent to the first one (Figure C6).

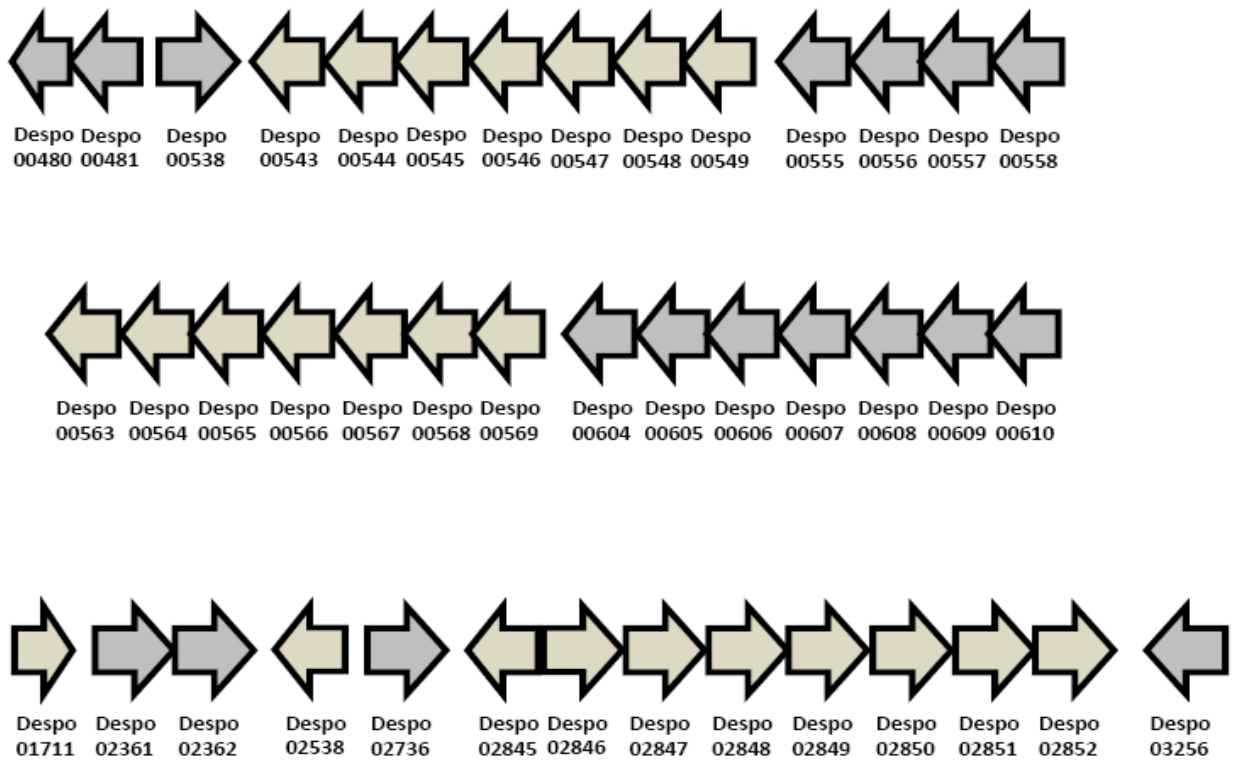


Figure C6: Two gene encoding flagella in the genome of *D. postgatei*. Cluster #1: DespoDRAFT\_00480, flagellar motor protein; DespoDRAFT\_00481, flagellar motor component; DespoDRAFT\_00538, flagellar protein FlaG; DespoDRAFT\_00543, flagellar basal-body P-ring protein; DespoDRAFT\_00544, flagellar basal body L-ring protein; DespoDRAFT\_00545, flagella basal body P-ring formation protein FlgA; DespoDRAFT\_00546, flagellar basal-body rod protein FlgG; DespoDRAFT\_00547, flagellar hook-basal body protein; DespoDRAFT\_00548, uncharacterized protein, cytoplasmic domain of flagellar protein FhlB like protein; DespoDRAFT\_00549, Flagellar hook-length control protein FliK; DespoDRAFT\_00555, flagellar GTP-binding protein; DespoDRAFT\_00556, flagellar biosynthesis protein FlhA; DespoDRAFT\_00557, flagellar biosynthetic protein FlhB; DespoDRAFT\_00558,

flagellar biosynthetic protein FliR; DespoDRAFT\_00563, flagellar biosynthetic protein FliQ; DespoDRAFT\_00564, flagellar biosynthetic protein FliP; DespoDRAFT\_00565, flagellar biosynthetic protein FliO; DespoDRAFT\_00566, flagellar motor switch protein FliN; DespoDRAFT\_00567, flagellar motor switch protein FliM; DespoDRAFT\_00568, flagellar basal body-associated protein; DespoDRAFT\_00569, flagellar hook-length control protein; DespoDRAFT\_00604, flagellar biosynthesis/type III secretory pathway protein; DespoDRAFT\_00605, flagellar motor switch protein FliG; DespoDRAFT\_00606, flagellar basal-body M-ring protein/flagellar hook-basal body protein FliF; DespoDRAFT\_00607, flagellar hook-basal body complex protein FliE; DespoDRAFT\_00608, flagellar basal-body rod protein FlgC; DespoDRAFT\_00609, flagellar basal-body rod protein FlgB; DespoDRAFT\_00610, response regulator with CheY-like receiver. Cluster #2: DespoDRAFT\_01711, Flagellar basal body-associated protein FliL; DespoDRAFT\_02361, flagellar motor component; DespoDRAFT\_02362, flagellar motor protein; DespoDRAFT\_02538, flagellar biosynthesis anti-sigma factor FlgM; DespoDRAFT\_02736, flagellar motor protein; DespoDRAFT\_02845, flagellin/flagellar hook associated protein; DespoDRAFT\_02846, flagellar capping protein; DespoDRAFT\_02847, flagellar biosynthetic protein FliS; DespoDRAFT\_02848, hypothetical protein; DespoDRAFT\_02849, flagellar protein FlaG; DespoDRAFT\_02850, hypothetical protein; DespoDRAFT\_02851, flagellar hook capping protein; DespoDRAFT\_02852, flagellar hook-basal body protein; DespoDRAFT\_03256, flagellar basal body rod protein

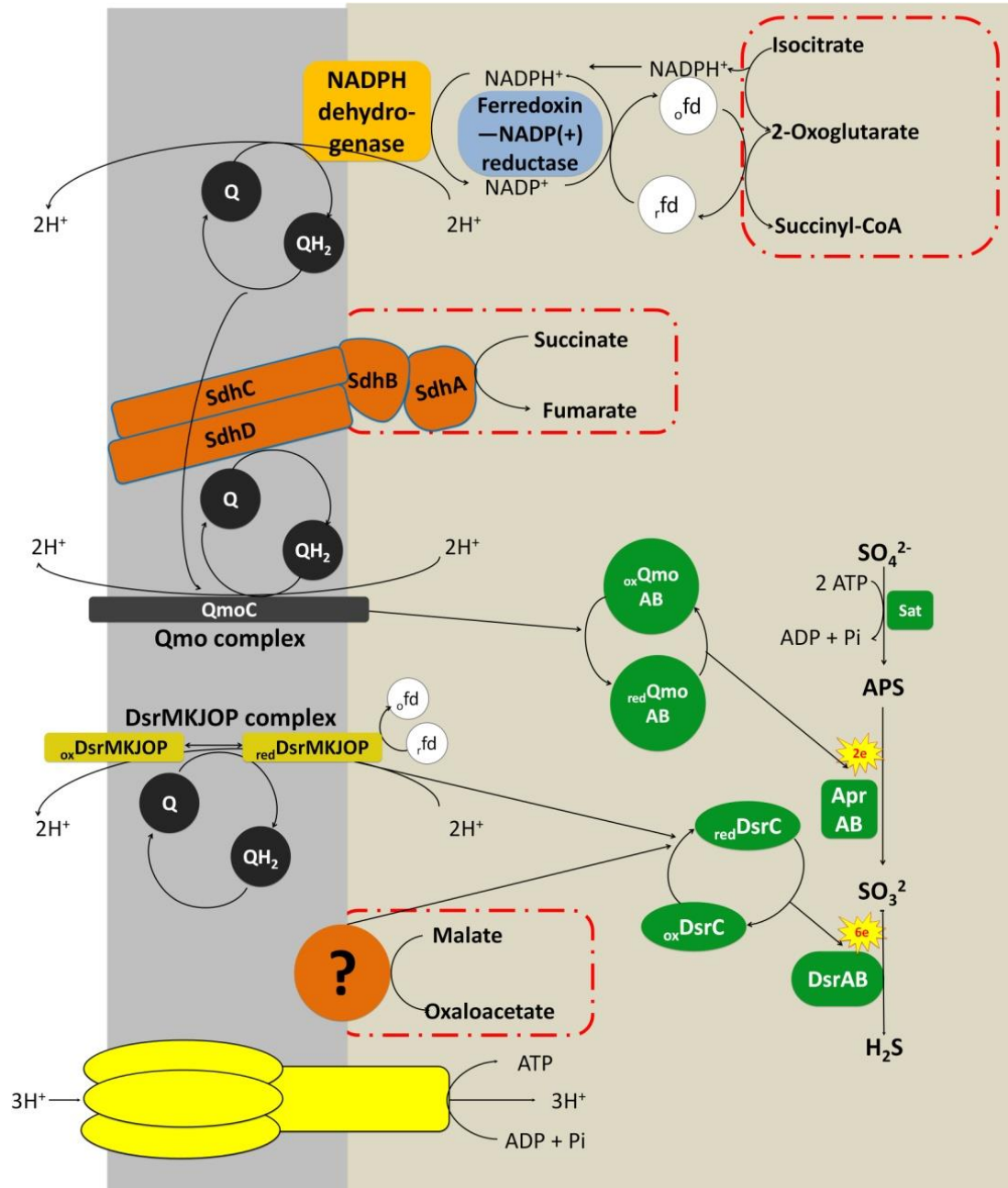


Figure C7: Schematic metabolic reconstruction of energy metabolism of *D. postgatei* based on biochemical experiments proposed by Rabus and colleagues (2006) (250). Red boxes indicate reactions that belong to the citric acid cycle. QH<sub>2</sub>: reduced quinone, Q: oxidized quinone, <sub>r</sub>ferr: reduced ferredoxin, and <sub>o</sub>ferr: oxidized ferredoxin.

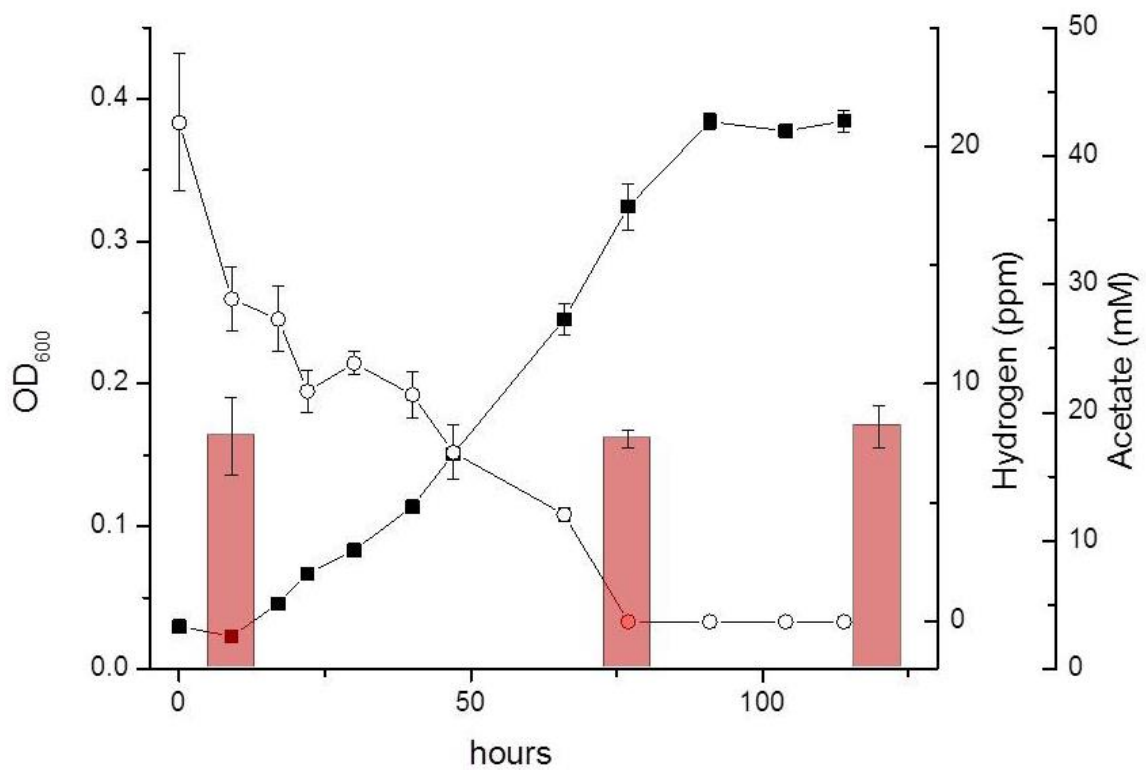


Figure C8: Acetate and hydrogen consumption by *D.postgatei*. Batch culture of *D.postgatei* using acetate (21 mM) and sulfate (20 mM) as electron donor and acceptor, respectively.

Table C2: Proton translocation and ATP production of sulfate reduction coupled to acetate oxidation in *D. postgatei*.

| Proton translocation                               | Per mol of acetate or sulfate | Comments   |
|--|-------------------------------|--|
| Sulfate transport                                  | 0 H <sup>+</sup>              | SRB membrane is not freely permeable to sulfate ions, sulfate is transported together with 2 Na <sup>+</sup> ions (244).   |
|  | -2 H <sup>+</sup>             | Under sulfate limitation, sulfate is transported together with 2 H <sup>+</sup> (241, 270).  |
| Acetate transport                                  | 0 H <sup>+</sup>              | Acetate freely diffuses across the membrane when acetate is abundant (243).  |
|  | -1 H <sup>+</sup>             | Under acetate limitation, acetate transport consumes 1 H <sup>+</sup> or Na <sup>+</sup> per acetate (229).  |
| Sulfate activation                                 | -2 ATP                        | 2 moles of ATP are required for the activation of sulfate to APS (153, 271).   |
| APS reduction                                      | +2 H <sup>+</sup>             | 1 H <sup>+</sup> per electron is translocated along APS reduction (2 electrons). Proton translocation across the membrane is driven by the membrane bound QmoC complex (229).  |
| Sulfite reduction                                  | +6 H <sup>+</sup>             | DsrMKJOP complex links reoxidation of membrane-bound quinones to proton translocation in ratio of 1H <sup>+</sup> per electron (272).  |
| Succinate oxidation                                | -2 H <sup>+</sup>             | Succinate oxidation to fumarate (E' = +0.033V) with menaquinone (E'=-0.074V) is endergonic. Therefore H <sup>+</sup> translocation from the periplasm served as a source of energy to carry out this reaction (250). |
| Ferredoxin oxidation – NADP <sup>+</sup> reduction | +2 H <sup>+</sup>             | RNF complex is predicted to translocate 2H <sup>+</sup> per ferredoxin reoxidized (229).   |
| NADH oxidation                                     | +1 to +2 H <sup>+</sup>       | Ehr complex is predicted to translocate 1-2 H <sup>+</sup> per ferredoxin reoxidized.  |

|  |                   |  |
|--|-------------------|--|
| N# protons translocated                        | +7 H <sup>+</sup> |  |
| N# ATP produced                                | 2.33              | We assumed that H <sup>+</sup> /ATP ratio of the <i>D.postgatei</i> ATP synthase is 3. |
| N# ATP consumed                                | -2                |  |
| Net ATP production by electron transport chain | 0.33              |  |
| Electron donor oxidation                       | +1                | ATP-citrate lyase produces 1 ATP via substrate level phosphorylation (153)             |
| ATP yield                                      | 1.33              |  |

### Calculations of *D.postgatei* Cell Composition

The shape of *D. postgatei* cell is reported to be rod shape to ellipsoidal cells with an average size of 1-1.5 by 1.7-2.5 μm with rounded ends (242). Therefore, assuming a radio of the volume of one cell is 0.75μm and 0.5μm, the volume of a single cell is 0.78 μm<sup>3</sup>.

$$Volumen = \frac{4}{3} \pi * a^2 * b ;$$

where *a* correspond to the radio of the minor axis, and *b* correspond to the radio of the major axis;

$$Volumen = \frac{4}{3} \pi * (0.5\mu m)^2 * 0.75\mu m$$

$$Volumen = 0.785 \mu m^3$$

Assuming that cell density of a cells is equal to the density of water = 1 g/ml, the mass of one cell of *D. postgatei* is

$$Mass = 1 \frac{g}{cm^3} * 0.785\mu m^3 * \left(\frac{1cm}{10mm}\right)^3 * \left(\frac{1mm}{1000\mu m}\right)^3$$

$$Mass = 7.85 * 10^{-13} \text{ g}$$

Since usually a bacterial cell has 70% of water (273), the dry weight of a single cell is  $2.35 * 10^{-13} \text{ g}$ .

The length of *D. postgatei* genome is 3,974,658 base pairs, and assuming that 1 base pair has a molecular weight of 666 g/mol, the molar mass of the genome is 2,647,122,228 g/mol. Since, 1 mole of nucleotides is equal to  $6.023 * 10^{23}$  molecules of nucleotides, the mass of the complete genome of *D.postgatei* is equal to  $4.39 * 10^{-15} \text{ g}$ . Therefore, the percentage of DNA in 1 gram of dry cell mass is

$$= \left( \frac{4.39 * 10^{-15} \text{ g}}{2.35 * 10^{-13} \text{ g}} * 100 \right) = 1.9\%$$

Table C3: Dry weighth of *D. postgatei* Culture

| Biomass (OD <sub>600</sub> ) | mgdw ml <sup>-1</sup> biomass |
|------------------------------|-------------------------------|
| 0.2                          | 0.037                         |
| 0.2                          | 0.050                         |
| 0.2                          | 0.034                         |
| 0.2                          | 0.030                         |
| 0.2                          | 0.027                         |
| Average                      | 0.036                         |



Table C4: Overall Macromolecular Composition of a *D. postgatei* Cell

| <b>Biomass component</b>                | <b>Percent (%)</b> |
|---|--------------------|
| Proteins                                | 53.1               |
| Lipids                                  | 5.5                |
| DNA                                     | 1.9                |
| RNA                                     | 15.3               |
| Carbohydrates (includes Glycogen)       | 14.1               |
| LPS                                     | 3.4                |
| Peptidoglycan (murein)                  | 2.5                |
| Cofactors, prosthetic groups and Others | 2.9                |
| Inorganic Ions                          | 1.4                |

Table C5: Protein Composition of 1 Gram of *D. postgatei* Cell

| Aminoacids    |     | count in genome | prevalence (P%) | MW (g/mol) | P * MW | % (by weight) | Content (mmol/gDW) |
|---------------|-----|-----------------|-----------------|------------|--------|---------------|--------------------|
| Alanine       | Ala | 93,198          | 8.0%            | 89.05      | 7.126  | 5.5%          | 0.358425385        |
| Arginine      | Arg | 59,189          | 5.1%            | 175.11     | 8.899  | 6.9%          | 0.227631925        |
| Asparagine    | Asn | 47,353          | 4.1%            | 132.05     | 5.369  | 4.1%          | 0.182112462        |
| Aspartic Acid | Asp | 67,251          | 5.8%            | 132.04     | 7.624  | 5.9%          | 0.258637155        |
| Cysteine      | Cys | 15,364          | 1.3%            | 121.02     | 1.596  | 1.2%          | 0.059087616        |
| Glutamic Acid | Glu | 71,752          | 6.2%            | 146.05     | 8.998  | 6.9%          | 0.275947319        |
| Glutamine     | Gln | 42,456          | 3.6%            | 146.07     | 5.325  | 4.1%          | 0.163279342        |
| Glycine       | Gly | 82,274          | 7.1%            | 75.03      | 5.300  | 4.1%          | 0.316413337        |
| Histidine     | His | 24,486          | 2.1%            | 155.07     | 3.260  | 2.5%          | 0.094169446        |
| Isoleucine    | Ile | 84,989          | 7.3%            | 131.07     | 9.564  | 7.4%          | 0.326854815        |
| Leucine       | Leu | 112,435         | 9.7%            | 131.09     | 12.655 | 9.8%          | 0.432407972        |
| Lysine        | lys | 75,414          | 6.5%            | 147.11     | 9.525  | 7.4%          | 0.290030816        |
| Methionine    | Met | 31,933          | 2.7%            | 149.05     | 4.087  | 3.2%          | 0.122809479        |
| Phenylalanine | Phe | 53,245          | 4.6%            | 165.08     | 7.547  | 5.8%          | 0.204772202        |
| proline       | Pro | 50,044          | 4.3%            | 115.06     | 4.944  | 3.8%          | 0.192461641        |
| Serine        | Ser | 69,185          | 5.9%            | 105.40     | 6.261  | 4.8%          | 0.266075026        |
| Threonine     | Thr | 62,587          | 5.4%            | 119.06     | 6.398  | 4.9%          | 0.240700118        |
| Tryptophan    | Trp | 12,000          | 1.0%            | 204.09     | 2.103  | 1.6%          | 0.046150182        |
| Tyrosine      | Tyr | 34,499          | 3.0%            | 181.07     | 5.363  | 4.1%          | 0.132677926        |

|        |     |             |        |         |       |        |             |
|--------|-----|-------------|--------|---------|-------|--------|-------------|
| Valine | Val | 75,037      | 6.4%   | 117.08  | 7.543 | 5.8%   | 0.288580931 |
| Sum    |     | 1,164,691.0 | 100.0% | 2,736.7 | 129.5 | 100.0% | 4.479225094 |

Table C6: Lipid composition of 1 gram of *D. postgatei* Cell.

| Name  | Formula            | Charge | Content<br>(g/gDW) | MW<br>(g/mol) | Content<br>(mmol/gDW) |
|---|--------------------|--------|--------------------|---------------|-----------------------|
| Fatty acid (Iso-C14:0)                        | C14H27O2           | -1     | 0.0046             | 227.3         | 0.001035476           |
| Iso-C14:0 CoA Isotetradecanoyl-CoA            | C35H59N7O17P3<br>S | -3     | 0.0046             | 241.3         | 0.001099253           |
| Fatty acid (Iso-C15:0)                        | C15H29O2           | -1     | 0.0046             | 241.39        | 0.001099663           |
| Iso-C15:0 CoA Isopentadecanoyl-CoA            | C36H61N7O17P3<br>S | -3     | 0.0046             | 988.8         | 0.004504524           |
| Fatty acid (Anteiso-C15:0)                    | C15H29O2           | -1     | 0.0046             | 241.39        | 0.001099663           |
| Anteiso-C15:0 CoA<br>Anteisopentadecanoyl-CoA | C36H61N7O17P3<br>S | -3     | 0.0046             | 988.8         | 0.004504524           |
| Fatty acid (iso-C16:0)                        | C16H31O2           | -1     | 0.0046             | 255.4         | 0.001163486           |
| Iso-C16:0 CoA Isohexadecanoyl-CoA             | C37H63N7O17P3<br>S | -3     | 0.0046             | 1005.9        | 0.004582424           |
| Fatty acid (Iso-C17:0)                        | C17H33O2           | -1     | 0.0046             | 269.44        | 0.001227446           |
| Iso-C17:0 CoA Isoheptadecanoyl-CoA            | C38H65N7O17P3<br>S | -3     | 0.0046             | 1016.946      | 0.004632744           |
| Fatty acid (Anteiso-C17:0)                    | C17H33O2           | -1     | 0.0046             | 269.44        | 0.001227446           |
| Anteiso-C17:0 CoA<br>Anteisoheptadecanoyl-CoA | C38H65N7O17P3<br>S | -3     | 0.0046             | 1016.946      | 0.004632744           |

Table C7: DNA composition of 1 gram of *D. postgatei* Cell.

| Component | Units in the genome | prevalence (P%) | MW (g/mol) | P * MW   | % (by weight) | Content (mmol/gDW) |
|-----------|---------------------|-----------------|------------|----------|---------------|--------------------|
| dATP      | 954,547             | 27.10           | 487.00     | 13195.39 | 27.3          | 0.010466           |
| dCTP      | 820,821             | 23.30           | 462.99     | 10787.39 | 22.3          | 0.008999           |
| dGTP      | 877,597             | 24.91           | 503.00     | 12530.24 | 25.9          | 0.009622           |
| dTTP      | 869,964             | 24.69           | 477.99     | 11803.65 | 24.4          | 0.009538           |
| Total     | 3,522,929           | 100             |            | 48316.66 | 100.0         | 0.0386             |

Table C8: RNA composition of 1 gram of *D. postgatei* Cell.

| Component | Units in the genome | prevalence (P%) | MW (g/mol) | P * MW   | % (by weight) | Content (mmol/gDW) |
|-----------|---------------------|-----------------|------------|----------|---------------|--------------------|
| ATP       | 869,964             | 24.69           | 503.00     | 12421.25 | 25.1          | 0.076155           |
| CTP       | 877,597             | 24.91           | 478.98     | 11931.87 | 24.1          | 0.076823           |
| GTP       | 820,821             | 23.30           | 518.99     | 12092.15 | 24.5          | 0.071853           |
| UTP       | 954,547             | 27.10           | 479.97     | 13004.92 | 26.3          | 0.083559           |
| Total     | 3,522,929           | 100             |            | 49450.19 | 100.0         | 0.3084             |

Table C9: Carbohydrate composition of 1 gram of *D. postgatei* Cell.

| Carbohydrate | Content<br>(g/gDW) | MW<br>(g/mol) | Content<br>(mmol/gDW) |
|--------------|--------------------|---------------|-----------------------|
| Ribose       | 0.013143           | 150.13        | 0.001973              |
| Heptose      | 0.013143           | 210.18        | 0.002762              |
| Glucose      | 0.013143           | 180.16        | 0.002368              |
| Galactose    | 0.013143           | 180.16        | 0.002368              |
| Rhamnose     | 0.013143           | 164.16        | 0.002158              |
| Glucosamine  | 0.013143           | 179.17        | 0.002355              |
| Glycogen     | 0.013143           | 666.5         | 0.00876               |
| Total        |                    |               | 0.02274               |

Table C10: Cofactor composition of 1 gram of *D. postgatei* Cell.

| Component                | Content (mmol/gDW) | Comments  |
|--------------------------|--------------------|---|
| Putrescine               | 0.0262             | Assumed to be the same quantities than <i>Dehalococcoides</i> model (188) |
| Homospermidine           | 0.0047             |   |
| Acetyl-CoA               | 0.0001             |   |
| CoA                      | 0.000006           |   |
| NAD                      | 3.547              |   |
| NADH                     | 3.547              |   |
| NADP                     | 0.000335           | Assumed to be the same quantities than 201165s3 <i>E.coli</i> model (274) |
| NADPH                    | 0.000112           |   |
| Succinyl-CoA             | 0.000003           | Assumed to be the same quantities than <i>Dehalococcoides</i> model (188) |
| AMP                      | 0.001              |   |
| ADP                      | 0.002              |   |
| ATP                      | 0.004              |   |
| 5,6,7,8-tetrahydrofolate | 0.0001             |   |
| Adenosylcobalamin        | 0.0047             |   |

Table C11: Murein composition of 1 gram of *D. postgatei* Cell.

| Compound ID            | Amount building block required ( $\mu\text{mol}$ ) | Content (g/gDW) | MW (g/mol) | Content (mmol/gDW) |
|------------------------|--|-----------------|------------|--------------------|
| <b>Building Blocks</b> |  |                 |            |                    |
| UDP-NAG                | 27.6   | 0.004166667     | 607        | 0.002529167        |
| UDP-NAM                | 27.6   | 0.004166667     | 607        | 0.002529167        |
| L-Alanine              | 27.6   | 0.004166667     | 89.05      | 0.000371042        |
| D-Alanine              | 27.6   | 0.004166667     | 89.05      | 0.000371042        |
| m-Diaminopimelic acid  | 27.6   | 0.004166667     | 190.2      | 0.0007925          |
| D-Glutamic acid        | 27.6   | 0.004166667     | 146.05     | 0.000608542        |



Table C12: LPS composition of 1 gram of *D. postgatei* Cell.

| Components                           | Amount building block required ( $\mu\text{mol}$ ) | Content (g/gDW) | MW (g/mol) | Content (mmol/gDW) |
|--------------------------------------|--|-----------------|------------|--------------------|
| Lipid A building blocks              |  |                 |            |                    |
| TDP-glucosamine                      | 15.7   | 0.003584956     | 179        | 0.000641707        |
| Fatty Acid -ACP (b-OH-myristic, etc) | 47   | 0.010732035     | 228.37     | 0.002450875        |
| CDP-ethanolamine                     | 7.8  | 0.001781061     | 446.24     | 0.000794781        |
| Core building blocks                 |  |                 |            |                    |
| CMP-KDO                              | 23.5   | 0.005366017     | 238.19     | 0.001278132        |
| ADP-heptose                          | 23.5   | 0.005366017     | 210.18     | 0.00112783         |
| UDP-glucose                          | 15.7   | 0.003584956     | 180.16     | 0.000645866        |
| CDP-ethanolamine                     | 15.7   | 0.003584956     | 61.08      | 0.000218969        |

Table C13: Energy Cost for processing and Polymerization of Macromolecules of bacterial cells

| Process  | mmol / gDW | mmol ATP / mmol <sup>a</sup> | mmol ATP / g DW |
|--|------------|------------------------------|-----------------|
| <b>Protein</b>                                   |            |                              |                 |
| Energy for activation and incorporation          | 4.479      | 4.000                        | 17.917          |
| Energy for mRNA synthesis                        |            | 0.200                        | 0.895           |
| Energy for proofreading                          |            | 0.100                        | 0.447           |
| Energy for assembly and modification             |            | 0.024                        | 0.108           |
| <b>Lipids</b>                                    |            |                              |                 |
| Energy for synthesis of phosphatidylethanolamine | 0.031      | 1.000                        | 0.031           |
| <b>DNA</b>                                       |            |                              |                 |
| Energy for unwinding the helix                   | 0.039      | 1.000                        | 0.039           |
| Energy for Proofreading                          |            | 0.350                        | 0.014           |
| Energy for discontinuous synthesis               |            | 0.006                        | 0.000           |
| Energy for negative supercoiling                 |            | 0.005                        | 0.000           |
| Energy for methylation                           |            | 0.001                        | 0.000           |
| <b>RNA</b>                                       |            |                              |                 |
| Energy for discarding segments                   | 0.308      | 0.380                        | 0.117           |
| Energy for modifications                         |            | 0.022                        | 0.007           |
| <b>Carbohydrates (includes Glycogen)</b>         |            |                              |                 |
| Energy for Synthesis of carbohydrates            | 0.023      | 8.000                        | 0.182           |
| <b>LPS</b>                                       |            |                              |                 |
| Energy for LPS assembly                          | 0.007      | 1.000                        | 0.007           |
| <b>Peptidoglycan (Murein)</b>                    |            |                              |                 |
| Energy for forming the pentapeptide              | 0.007      | 0.833                        | 0.006           |
| <b>Total Cost</b>                                |            |                              | 19.7698         |

Table C14: Biosynthetic Cost of making 1 mmol of each of these building blocks (mmol/mmol)

| Building block | quantity in 1 g dried cells (mmol/gDW) | Cost of making 1 mmol of each of these building blocks (mmol/mmol) |             |                |            |               |              |
|----------------|--|--|-------------|----------------|------------|---------------|--------------|
|                |  | ATP/<br>mmol   | ATP         | NADPH/<br>mmol | NADPH      | NADH<br>/mmol | NADH         |
| Alanine        | 0.358425385                            | 0  | 0           | 1              | 0.35842538 | 0             | 0            |
| Arginine       | 0.227631925                            | 7  | 1.593423474 | 4              | 0.91052769 | -1            | -1.593423474 |
| Asparagine     | 0.182112462                            | 3  | 0.546337387 | 1              | 0.18211246 | 0             | 0            |
| Aspartic Acid  | 0.258637155                            | 0  | 0           | 1              | 0.25863715 | 0             | 0            |
| Cysteine       | 0.059087616                            | 4  | 0.236350463 | 5              | 0.29543807 | -1            | -0.236350463 |
| Glutamic Acid  | 0.275947319                            | 0  | 0           | 1              | 0.27594731 | 0             | 0            |
| Glutamine      | 0.163279342                            | 1  | 0.163279342 | 1              | 0.16327934 | 0             | 0            |
| Glycine        | 0.316413337                            | 0  | 0           | 1              | 0.31641333 | -1            | 0            |
| Histidine      | 0.094169446                            | 6  | 0.565016673 | 1              | 0.09416944 | -3            | -1.695050019 |
| Isoleucine     | 0.326854815                            | 2  | 0.65370963  | 5              | 1.63427407 | 0             | 0            |
| Leucine        | 0.432407972                            | 0  | 0           | 2              | 0.86481594 | -1            | 0            |
| Lysine         | 0.290030816                            | 2  | 0.580061632 | 4              | 1.16012326 | 0             | 0            |
| Methionine     | 0.122809479                            | 7  | 0.859666353 | 8              | 0.98247583 | 0             | 0            |
| Phenylalanine  | 0.204772202                            | 1  | 0.204772202 | 2              | 0.40954440 | 0             | 0            |
| proline        | 0.192461641                            | 1  | 0.192461641 | 3              | 0.57738492 | 0             | 0            |
| Serine         | 0.266075026                            | 0  | 0           | 1              | 0.26607502 | -1            | 0            |
| Threonine      | 0.240700118                            | 2  | 0.481400236 | 3              | 0.72210035 | 0             | 0            |

|                     |             |      |             |    |            |    |              |
|---------------------|-------------|------|-------------|----|------------|----|--------------|
| Tryptophan          | 0.046150182 | 5    | 0.230750908 | 3  | 0.13845054 | -2 | -0.461501816 |
| Tyrosine            | 0.132677926 | 1    | 0.132677926 | 2  | 0.26535585 | -1 | -0.132677926 |
| Valine              | 0.288580931 | 0    | 0           | 2  | 0.57716186 | 0  | 0            |
| SubTotal            |             |      | 6.439907867 |    | 10.4527123 |    | -4.119003698 |
| RNA nucleotides     |             |      |             |    |            |    |              |
| ATP                 | 0.076155147 | 11   | 0.837706619 | 1  | 0.07615514 | -3 | -0.228465441 |
| CTP                 | 0.076823327 | 13   | 0.998703248 | 0  | 0          | -3 | -0.23046998  |
| GTP                 | 0.071853254 | 9    | 0.646679284 | 1  | 0.07185325 | 0  | 0            |
| UTP                 | 0.083559397 | 7    | 0.584915779 | 1  | 0.08355939 | 0  | 0            |
| SubTotal            |             |      | 3.068004929 |    | 0.23156779 |    | -0.458935422 |
| DNA nucleotides     |             |      |             |    |            |    |              |
| dATP                | 0.010465663 | 11   | 0.115122288 | 2  | 0.02093132 | -3 | -0.031396988 |
| dCTP                | 0.008999489 | 13   | 0.116993362 | 1  | 0.00899948 | -3 | -0.026998468 |
| dGTP                | 0.009621982 | 9    | 0.086597838 | 2  | 0.01924396 | 0  | 0            |
| dTTP                | 0.009538294 | 10.5 | 0.100152084 | 3  | 0.02861488 | 0  | 0            |
| SubTotal            |             |      | 0.418865571 |    | 0.07778965 |    | -0.058395456 |
| Lipid components    |             |      |             |    |            |    |              |
| total fatty acids   | 0.030809395 | 7.2  | 0.221827645 | 14 | 0.43133153 | 0  | 0            |
|                     |             |      | 0.221827645 |    | 0.43133153 |    | 0            |
| LPS components      |             |      |             |    |            |    |              |
| TDP-glucosamine     | 0.000641707 | 2    | 0.001283414 | 0  | 0          | 0  | 0            |
| Fatty Acid -ACP (b- | 0.002450875 | 6    | 0.014705249 | 11 | 0.02695962 | 0  | 0            |

|                       |             |   |             |    |            |    |              |
|-----------------------|-------------|---|-------------|----|------------|----|--------------|
| OH-myristic, etc)     |             |   |             |    |            |    |              |
| CDP-ethanolamine      | 0.000794781 | 3 | 0.002384342 | 1  | 0.00079478 | -1 | -0.000794781 |
| CMP-KDO               | 0.001278132 | 2 | 0.002556263 | 0  | 0          | 0  | 0            |
| ADP-heptose           | 0.00112783  | 1 | 0.00112783  | -4 | -0.0045113 | 0  | 0            |
| UDP-glucose           | 0.000645866 | 1 | 0.000645866 | 0  | 0          | 0  | 0            |
| CDP-ethanolamine      | 0.000218969 | 3 | 0.000656907 | -1 | -0.0002189 | 1  | 0.000218969  |
| SubTotal              |             |   | 0.023359871 |    | 0.02302411 |    | -0.000575812 |
| Murein components     |             |   |             |    |            |    |              |
| UDP-NAG               | 0.002529167 | 3 | 0.0075875   | 0  | 0          | 0  | 0            |
| UDP-NAM               | 0.002529167 | 4 | 0.010116667 | 1  | 0.00252916 | 0  | 0            |
| L-Alanine             | 0.000371042 | 0 | 0           | 0  | 0          | 1  | 0.000371042  |
| D-Alanine             | 0.000371042 | 0 | 0           | 0  | 0          | 1  | 0.000371042  |
| m-Diaminopimelic acid | 0.0007925   | 2 | 0.001585    | 3  | 0.0023775  | 0  | 0            |
| D-Glutamic acid       | 0.000608542 | 0 | 0           | 0  | 0          | 1  | 0.000608542  |
|                       |             |   | 0.019289167 |    | 0.00490666 |    | 0.001350625  |
| Carbohydrates         |             |   |             |    |            |    |              |
| Ribose                | 0.001973137 | 1 | 0.001973137 | 0  | 0          | 0  | 0            |
| Heptose               | 0.002762366 | 1 | 0.002762366 | 0  | 0          | 0  | 0            |
| Glucose               | 0.002367817 | 1 | 0.002367817 | 0  | 0          | 0  | 0            |
| Galactose             | 0.002367817 | 1 | 0.002367817 | 0  | 0          | 0  | 0            |
| Rhamnose              | 0.002157531 | 1 | 0.002157531 | 0  | 0          | 0  | 0            |
| Glucosamine           | 0.002354806 | 1 | 0.002354806 | 0  | 0          | 0  | 0            |

|          |             |   |             |   |            |   |              |
|----------|-------------|---|-------------|---|------------|---|--------------|
| Glycogen | 0.008759714 | 1 | 0.008759714 | 0 | 0          | 0 | 0            |
| SubTotal |             |   | 0.022743189 |   | 0          |   | 0            |
|          |             |   | ATP         |   | NADPH      |   | NADH         |
| Total    |             |   | 10.21399824 |   | 11.2213320 |   | -4.635559762 |

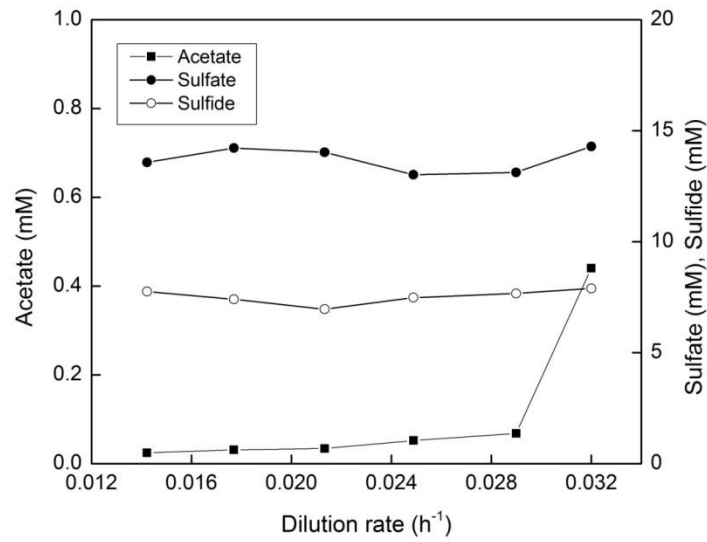


Figure C9: Influence of the growth rate on steady state values of acetate concentration (close squares), sulfate concentration (closed circles), and sulfide concentration (open circles) in acetate-limiting chemostats under sulfate reduction.

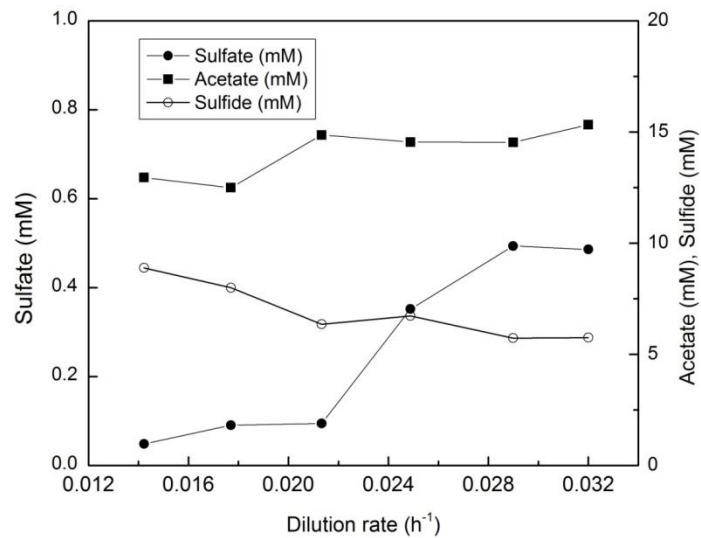


Figure C10: Influence of the growth rate on steady state values of acetate concentration (close squares), sulfate concentration (closed circles), and sulfide concentration (open circles) in sulfate-limiting chemostats under sulfate reduction.

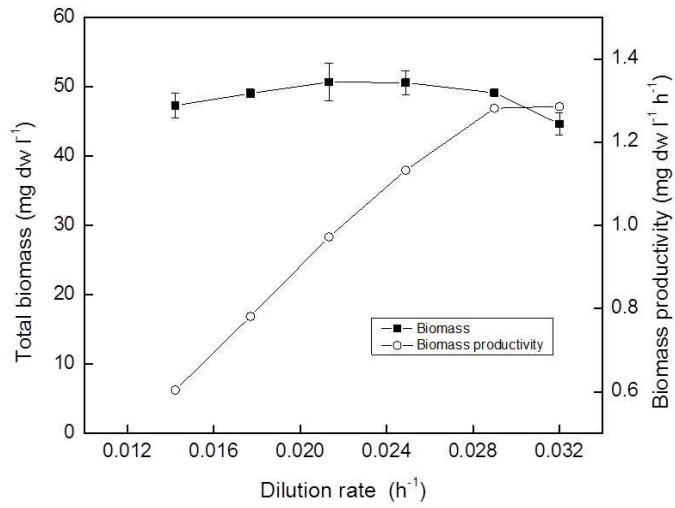


Figure C11: Influence of the growth rate on steady state values of biomass (close squares) and biomass productivity (open circles) in acetate-limiting chemostats under sulfate reduction.

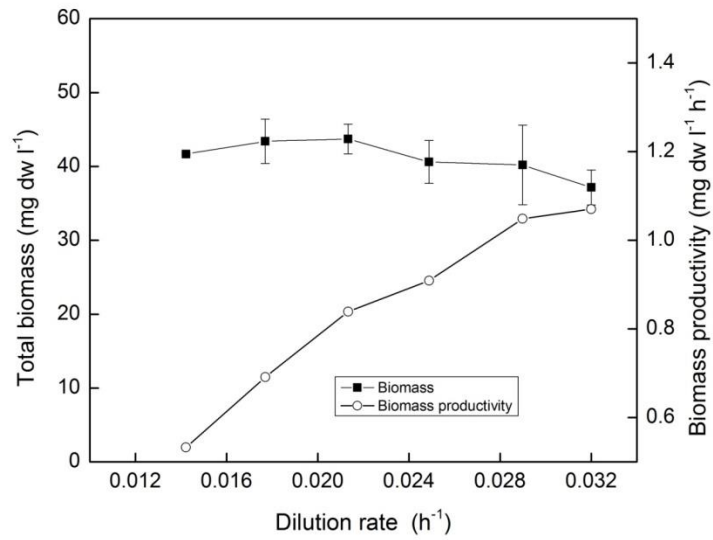


Figure C12: Influence of the growth rate on steady state values of biomass (close squares) and biomass productivity (open circles) in sulfate-limiting chemostats under sulfate reduction.



Table C15: Total biomass, biomass productivity, specific respiration rates and Yield in acetate-limited chemostats.

| D (hr <sup>-1</sup> ) | Total biomass (mg dw/l) | Biomass productivity (mg dw/l h) | Acetate assimilated (%) | Acetate dissimilated (%) | q <sub>acetate</sub> (mmol acetate/g dw h) | q <sub>sulfate</sub> (mmol SO <sub>4</sub> /g dw h) | Y <sub>acetate</sub> (mg dw/mM consumed) | Y <sub>sulfate</sub> (mg dw/mM consumed) |
|-----------------------|-------------------------|----------------------------------|-------------------------|--------------------------|--|---|--|--|
| 0.032                 | 44.646                  | 1.286                            | 11.32%                  | 88.68%                   | 5.1988                                     | 4.4040  | 5.54                                     | 6.54                                     |
| 0.029                 | 49.125                  | 1.282                            | 11.91%                  | 88.09%                   | 4.4776                                     | 4.2449  | 5.83                                     | 6.15                                     |
| 0.025                 | 50.576                  | 1.132                            | 12.24%                  | 87.76%                   | 3.7401                                     | 3.5885  | 5.99                                     | 6.24                                     |
| 0.021                 | 50.671                  | 0.973                            | 12.23%                  | 87.77%                   | 3.2067                                     | 2.6842  | 5.99                                     | 7.15                                     |
| 0.018                 | 49.044                  | 0.781                            | 11.84%                  | 88.16%                   | 2.7508                                     | 2.2414  | 5.79                                     | 7.11                                     |
| 0.014                 | 47.286                  | 0.604                            | 11.40%                  | 88.60%                   | 2.2906                                     | 2.0394  | 5.58                                     | 6.27                                     |

Table C16: Total biomass, biomass productivity, specific respiration rates and Yield in sulfate-limited chemostats.

| D (hr <sup>-1</sup> ) | Total biomass (mg dw/l) | Biomass productivity (mg dw/l h) | Acetate assimilated (%) | Acetate dissimilated (%) | q <sub>acetate</sub> (mmol acetate/g dw h) | q <sub>sulfate</sub> (mmol SO <sub>4</sub> /g dw h) | Y <sub>acetate</sub> (mg dw/mM consumed) | Y <sub>sulfate</sub> (mg dw/mM consumed) |
|-----------------------|-------------------------|----------------------------------|-------------------------|--------------------------|--|---|--|--|
| 0.032                 | 37.158                  | 1.070                            | 13.11%                  | 86.89%                   | 4.4886                                     | 6.2114  | 6.42                                     | 4.64                                     |
| 0.029                 | 40.199                  | 1.049                            | 12.49%                  | 87.51%                   | 4.2692                                     | 5.1958  | 6.11                                     | 5.02                                     |
| 0.025                 | 40.604                  | 0.909                            | 12.64%                  | 87.36%                   | 3.6214                                     | 4.4934  | 6.18                                     | 4.98                                     |
| 0.021                 | 43.724                  | 0.839                            | 14.30%                  | 85.70%                   | 2.7432                                     | 3.6897  | 7.00                                     | 5.20                                     |
| 0.018                 | 43.397                  | 0.691                            | 10.29%                  | 89.71%                   | 3.1642                                     | 3.0867  | 5.03                                     | 5.16                                     |
| 0.014                 | 41.679                  | 0.533                            | 10.43%                  | 89.57%                   | 2.5045                                     | 2.5915  | 5.10                                     | 4.93                                     |

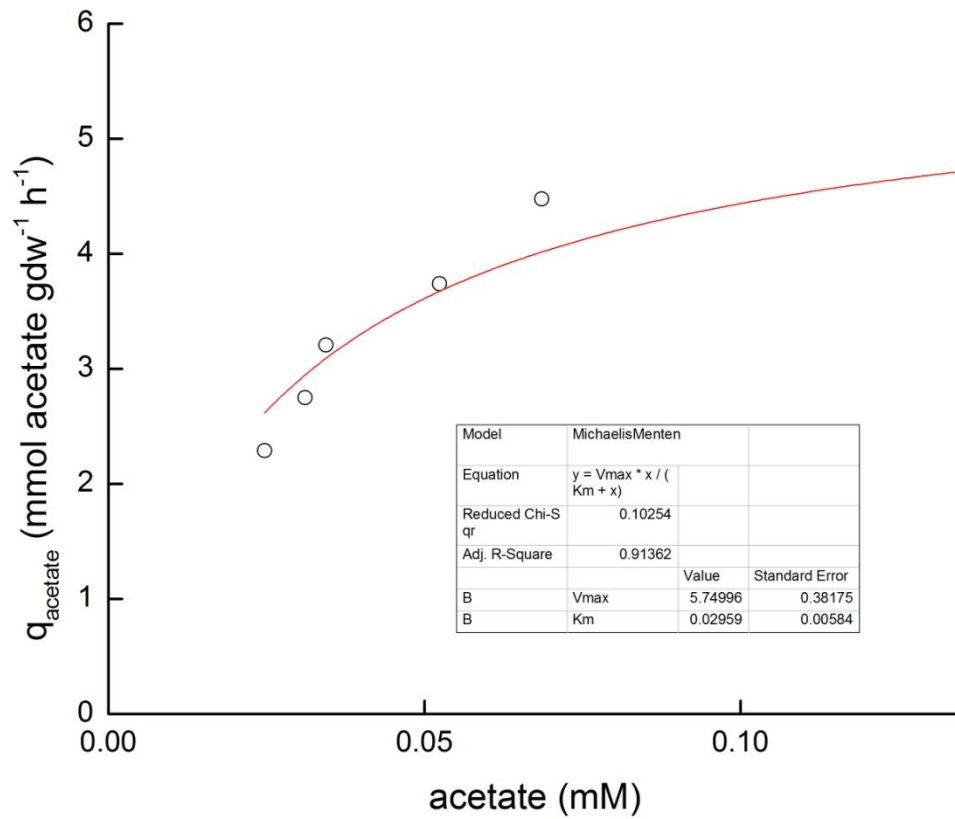


Figure C13: Michaelis-Menten type relationship that represents the effect of acetate concentrations and specific acetate consumption rates under acetate-limited conditions. Each point represents the average of triplicate measurements

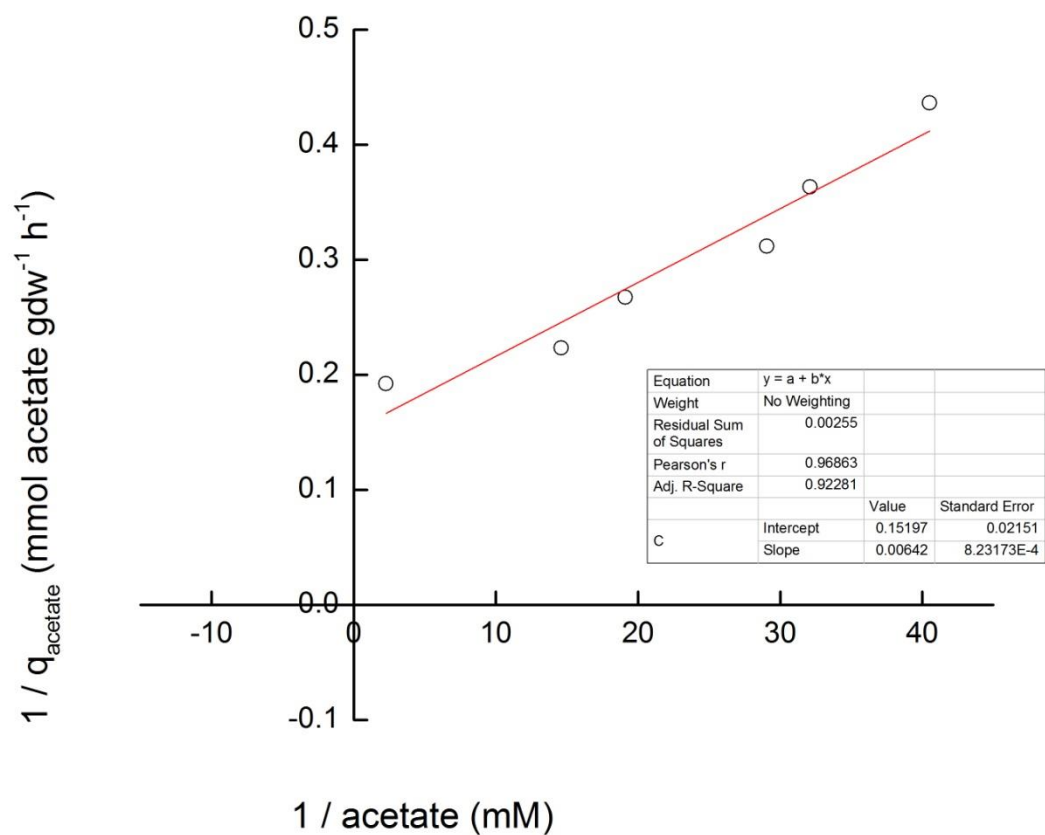


Figure C14: Lineweaver-Burk Linearization plot of the same data as Figure C13.

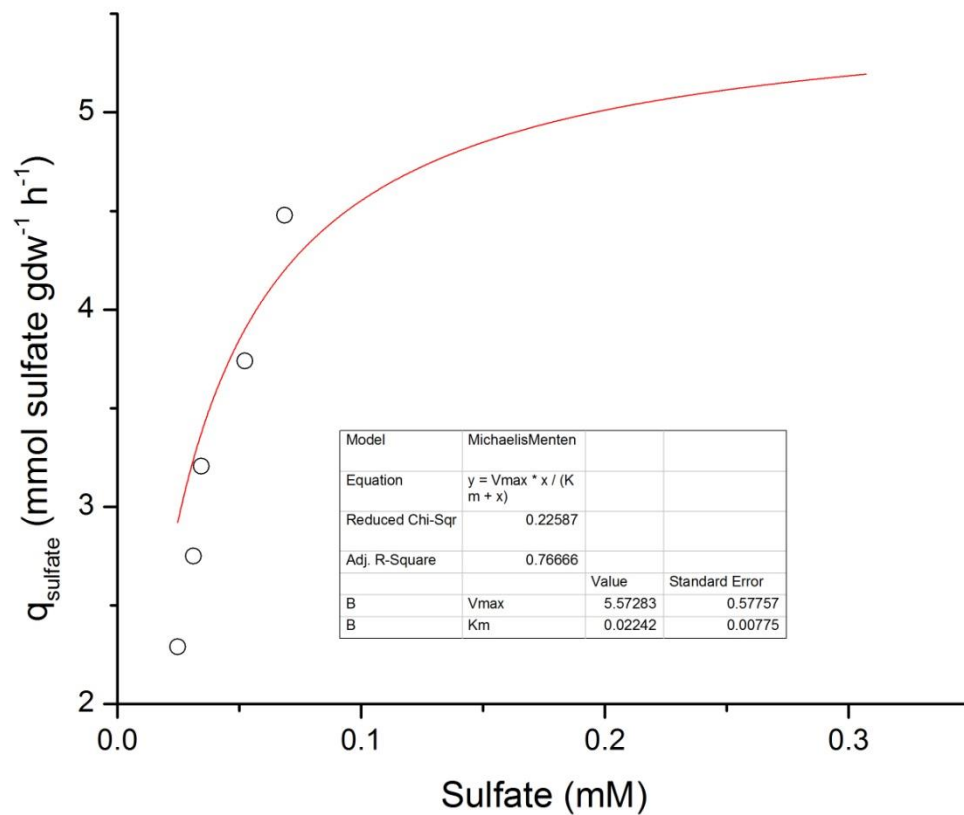


Figure C15: Michaelis-Menten type relationship that represents the effect of sulfate concentrations and specific sulfate consumption rates under sulfate-limited conditions. Each point represents the average of triplicate measurements.

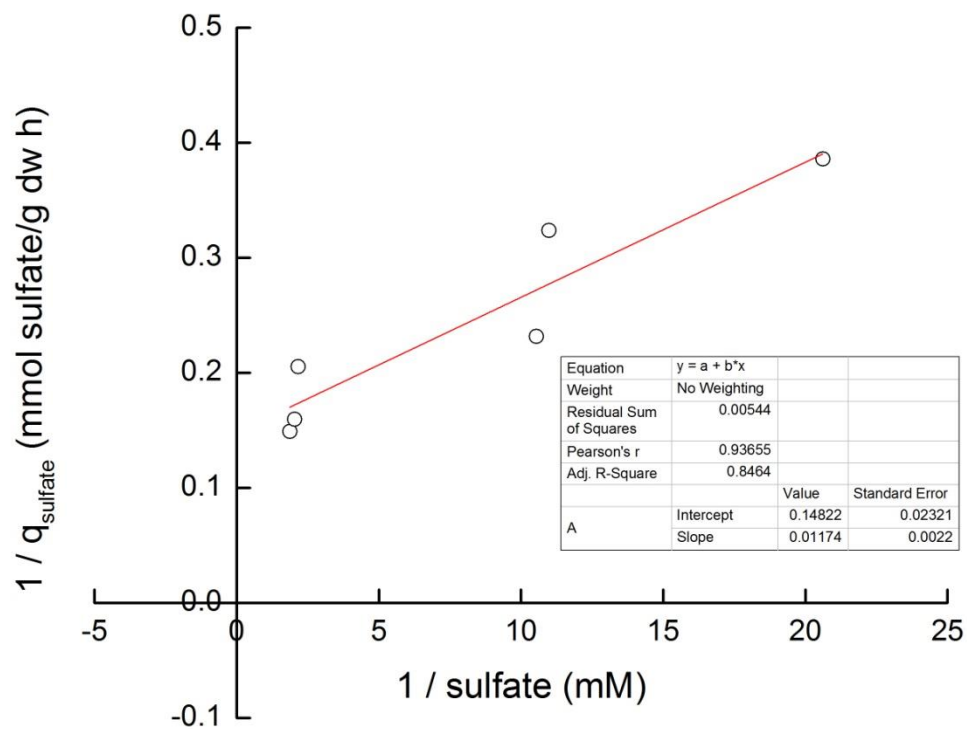


Figure C16: Lineweaver-Burk Linearization plot of the same data as Figure C15.

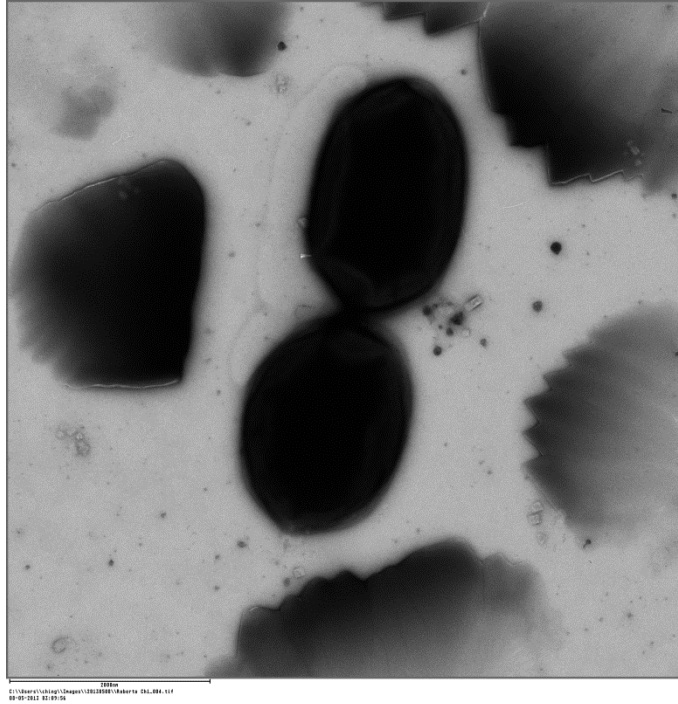


Figure C17: Transmission Electron Microscopy image of *D.postgatei* during growth in acetate-limiting chemostats at  $D= 0.032 \text{ h}^{-1}$

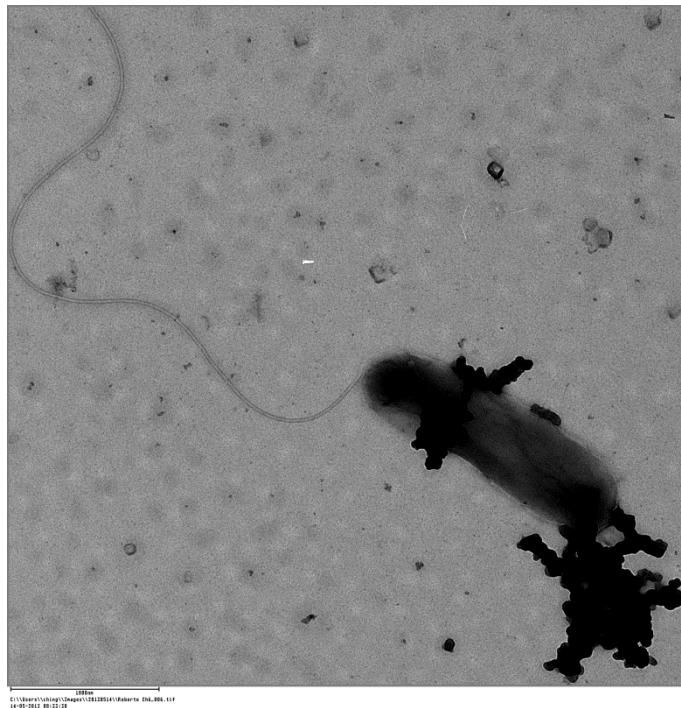


Figure C18: Transmission Electron Microscopy image of *D.postgatei* during growth in acetate-limiting chemostats at  $D= 0.014 \text{ h}^{-1}$

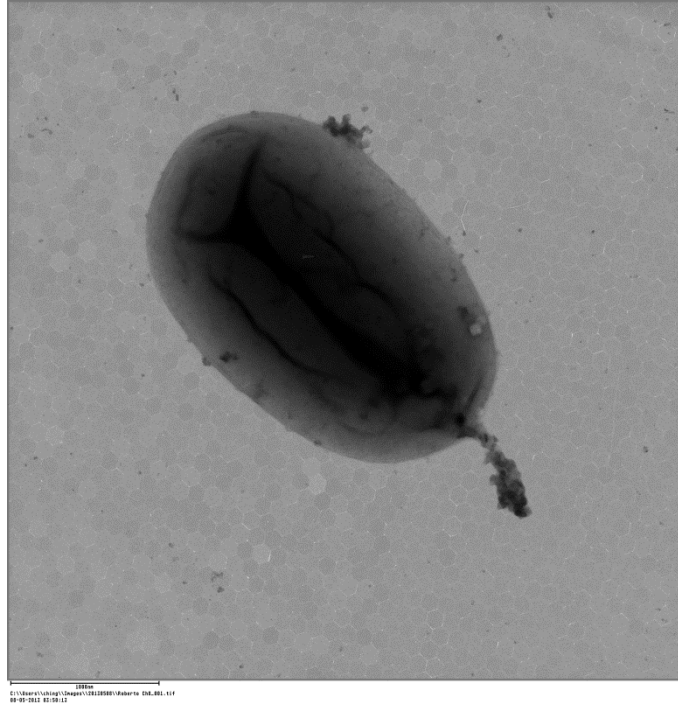


Figure C19: Transmission Electron Microscopy image of *D. postgatei* during growth in sulfate-limiting chemostats at  $D= 0.032 \text{ h}^{-1}$

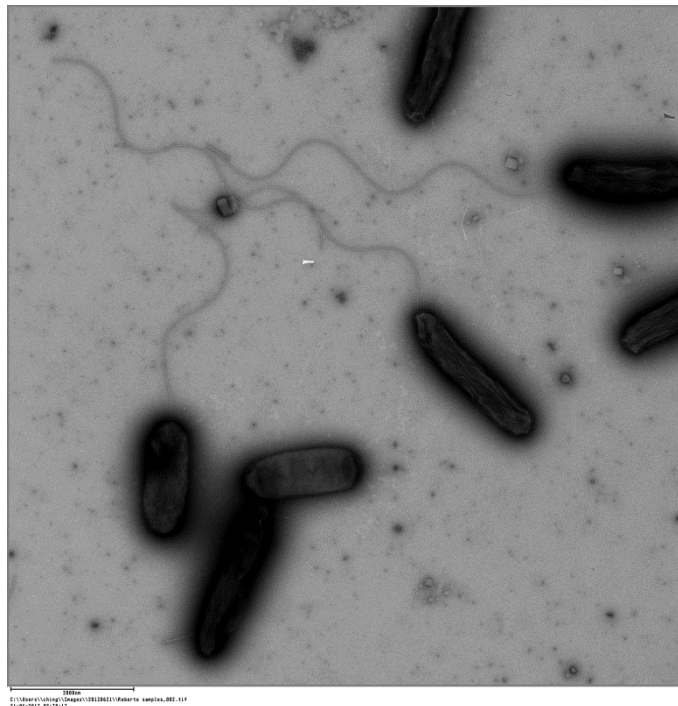


Figure C20: Transmission Electron Microscopy image of *D. postgatei* during growth in sulfate-limiting chemostats at  $D= 0.014 \text{ h}^{-1}$



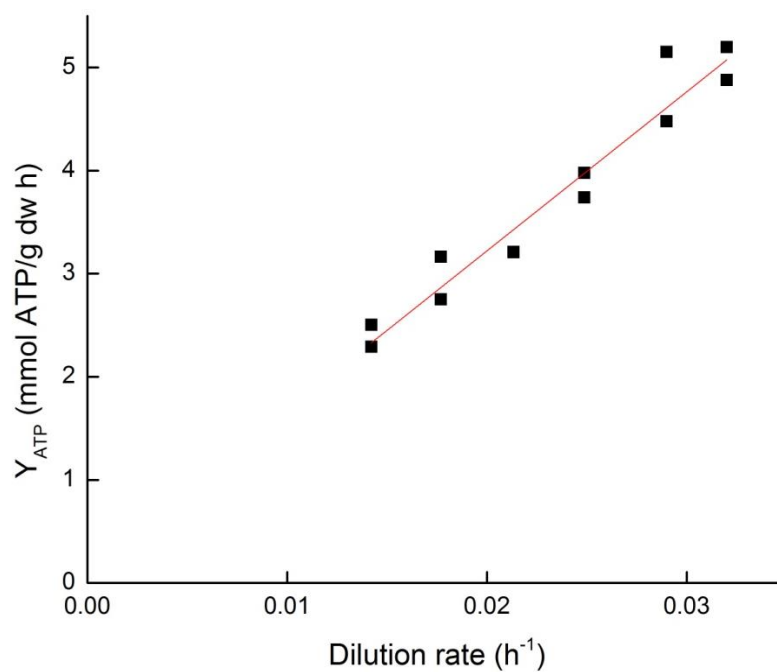


Figure C21:  $Y_{\text{ATP}}$  values of continuous cultures of *D.postgatei* during growth in both acetate and sulfate-limiting conditions. A projection drawn from the correlation to the Y-axis indicates the quantity of energy that is devoted to NGAM (Non-Growth Associated Maintenance energy).

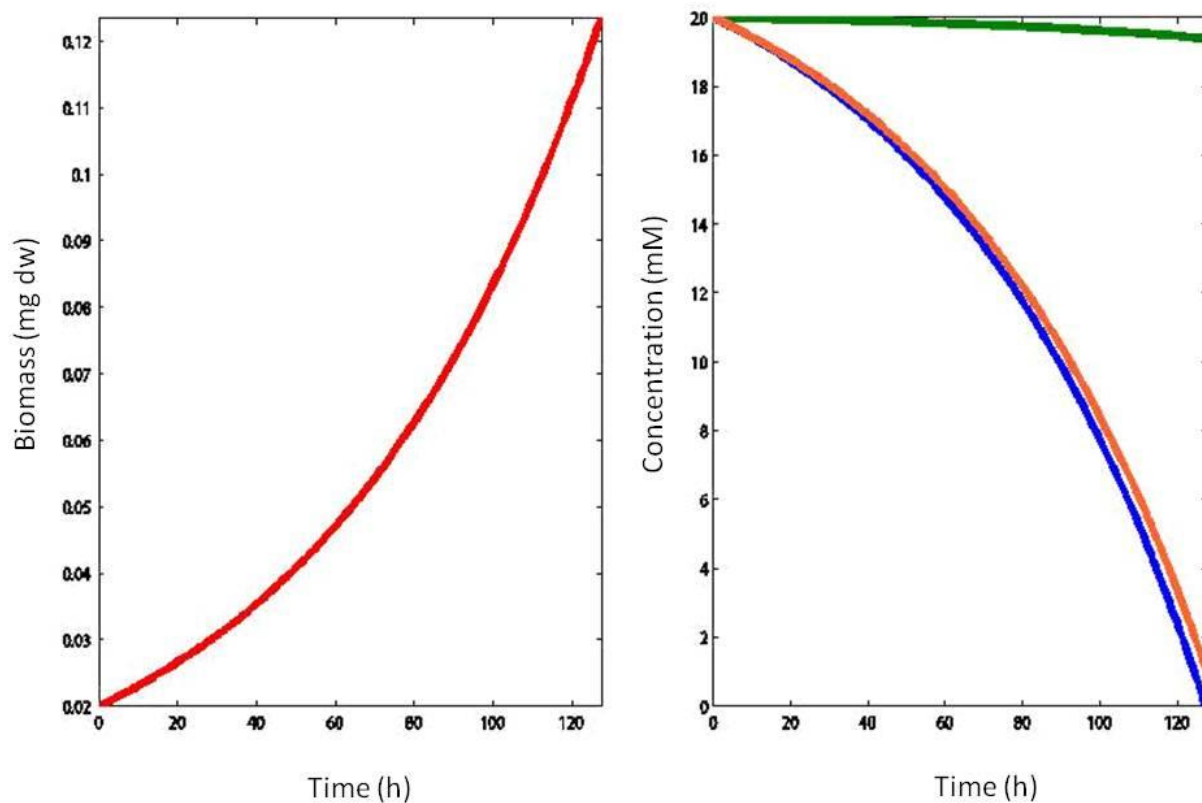


Figure C22: Dynamic flux balance analysis of *D.postgatei* model. The left graph indicates the biomass generation (red) and the right the acetate (blue), sulfate (orange), and ammonia (green) concentrations as a function of time.

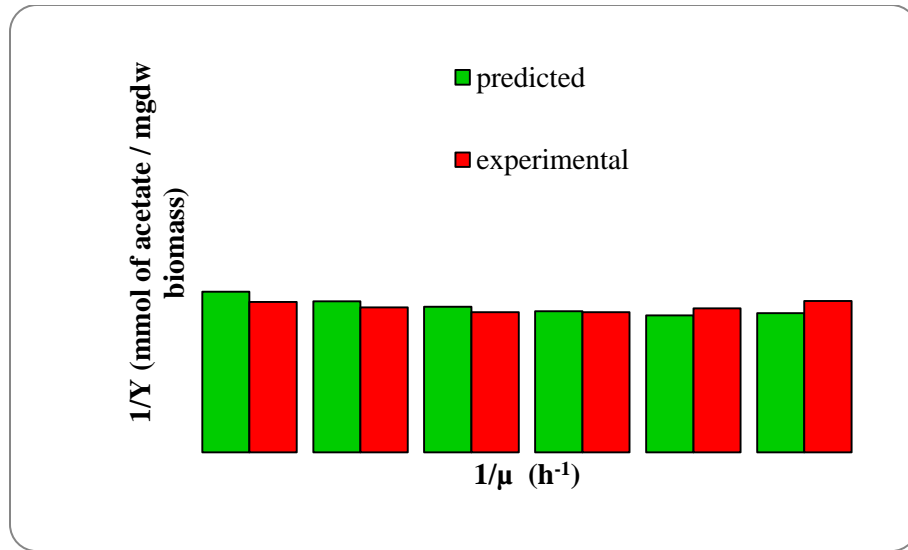


Figure C23: Validation of the *D.postgatei* metabolic model with experimental data. Reciprocal plot of predicted and experimental growth yields (1/Y) versus growth rates (1/μ) in acetate limited chemostats.

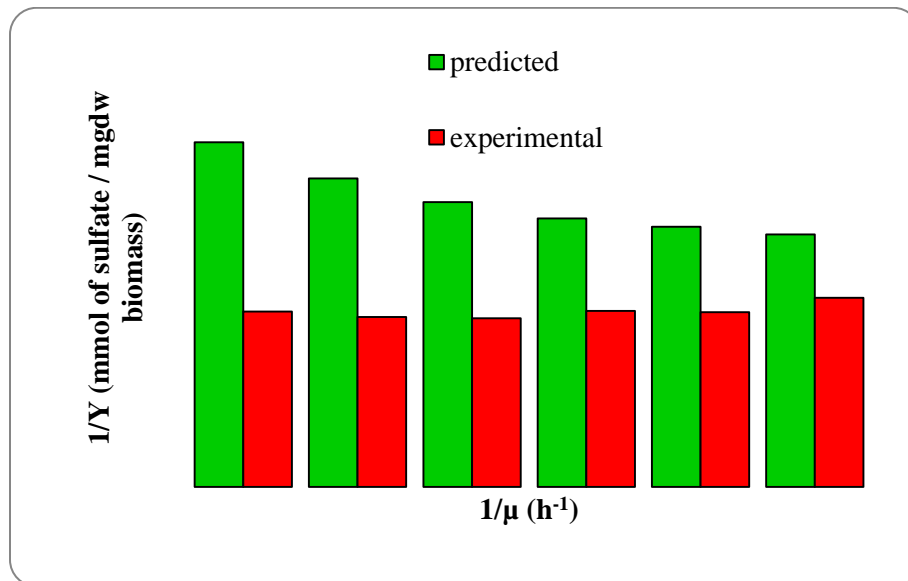


Figure C24: Validation of the *D.postgatei* metabolic model with experimental data. Reciprocal plot of predicted and experimental growth yields (1/Y) versus growth rates (1/μ) in sulfate limited chemostats.

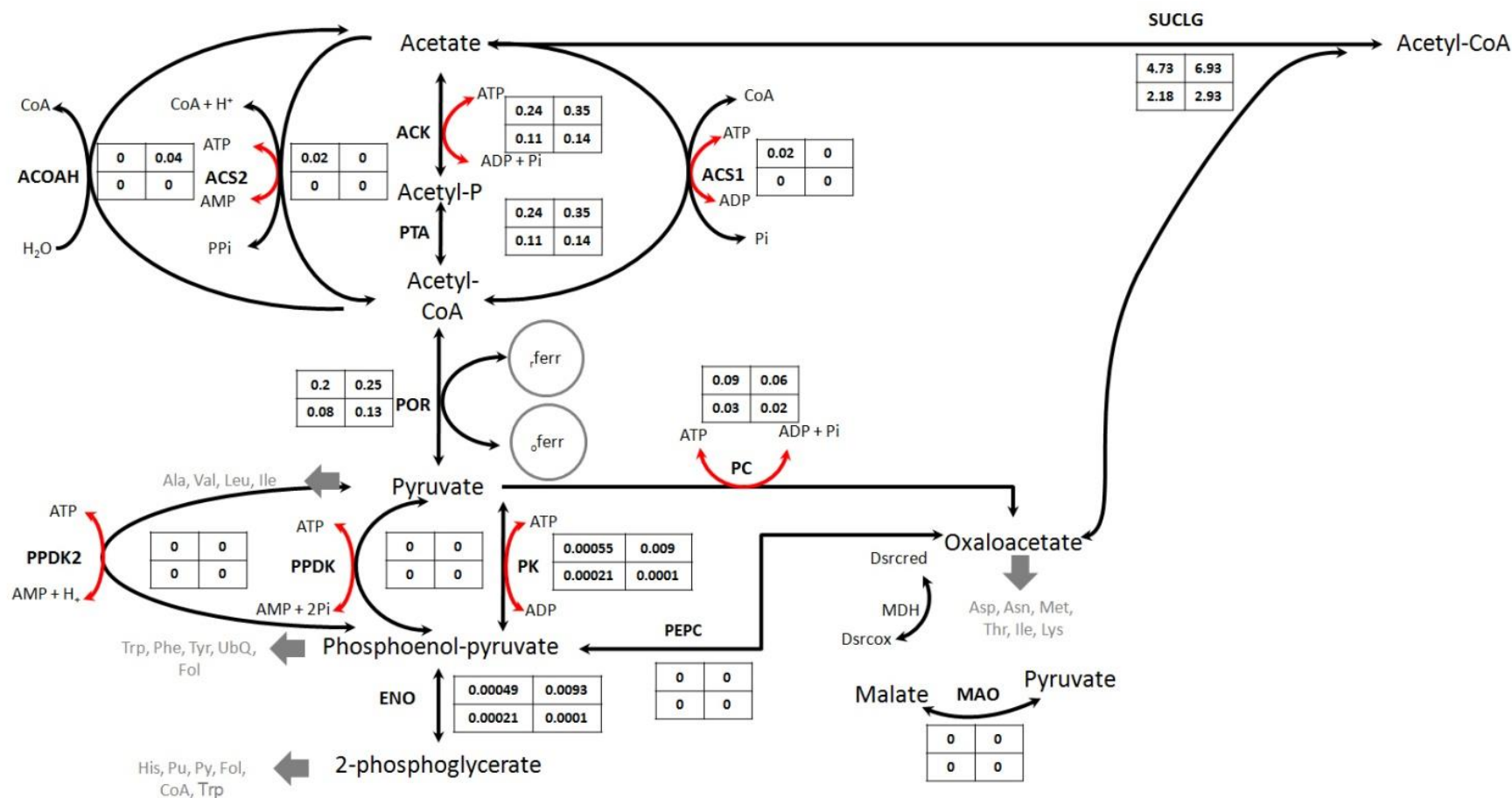


Figure C25: *In silico* flux estimation of a set of reactions responsible for acetate oxidation. The boxes besides the reactions correspond to the flux predicted per each reaction (mmol/gdw h) for *D. postgatei* cultures growing in chemostats. The numbers on the left column of the boxes correspond to acetate limited cultures growing at  $D= 0.032 \text{ h}^{-1}$  (up) and  $D= 0.014 \text{ h}^{-1}$  (down). The numbers on the right column correspond to sulfate limited cultures growing at  $D= 0.032 \text{ h}^{-1}$  (up) and  $D= 0.014 \text{ h}^{-1}$  (down). Abbreviations are the following: ACK, Acetate kinase; ACS1, Acetate-CoA ligase (ADP-forming); ACS2, Acetate-CoA ligase

(AMP-forming); POR, Pyruvate ferredoxin oxidoreductase; PK, Pyruvate kinase; PPDK, Pyruvate phosphate dikinase; PPDK2, Phosphoenolpyruvate synthase; PEPC, Phosphoenolpyruvate carboxylase; ENO, Enolase; MDH, Malate dehydrogenase ; MAO, Malate oxidoreductase, and SUCLG, Succinyl:acetate CoA transferase.

Note: for Figures C26 to C37, the numbers inside each metabolic representation indicate (1) citric acid cycle, (2) sulfate reduction pathway, (3) anapleurotic reactions, (4) ATP synthase, (5) Qrc (Quinone-reductase) complex, (6) Ehr (Ech-hydrogenase-related) complex, (7) Rnf (H<sup>+</sup>-translocating ferredoxin:NADP<sup>+</sup> oxidoreductase) and Nfn (Ferredoxin:NADP oxidoreductase) complex. Abbreviations are the following: atp, ATP; 3pg, 3-Phospho-D-glycerate; 13dpg, 3-Phospho-D-glyceroyl phosphate; adp, ADP; ru5p-D, D-Ribulose 5-phosphate; n2, nitrogen; pan, Pantothenate; 2pg, D-Glycerate 2-phosphate; ac, Acetate; accoa, Acetyl-CoA; acon-C, cis-Aconitate; actp, Acetyl phosphate; adp, ADP; akg, 2-Oxoglutarate; amp, Adenosine Monophosphate; aps, Adenosine 5'-phosphosulfate; cit, Citrate; co2, carbon dioxide; coa, Coenzyme A; dhap, Dihydroxyacetone phosphate; DsrCred, DsrC cytochrome - reduced; DsrCrox, DsrC cytochrome - oxidized; e4p, D-Erythrose 4-phosphate; f6p, D-Fructose 6-phosphate; Fdox, Oxidized ferredoxin; fdp, D-Fructose 1,6-bisphosphate; Fdred, Reduced ferredoxin; fol, folate; for, Formate; fum, Fumarate; g3p, Glyceraldehyde 3-phosphate; glu-L, L-Glutamate; h, H<sup>+</sup>; h2o, H<sub>2</sub>O; h2s, H<sub>2</sub>S; icit, Isocitrate; mal-L, L-Malate; mk, Quinone; mkh2, Quinol; nad, Nicotinamide adenine dinucleotide; nadh, Nicotinamide adenine dinucleotide - reduced; nadp, Nicotinamide adenine dinucleotide phosphate; nadph, Nicotinamide adenine dinucleotide phosphate - reduced; nh4, Ammonium; oaa, Oxaloacetate; pep, Phosphoenolpyruvate; pi, Phosphate; pyr, Pyruvate; r5p, alpha-D-Ribose 5-phosphate; s7p, Sedoheptulose 7-phosphate; so3, SO<sub>3</sub>; so4, SO<sub>4</sub>; succ, Succinate; succoa, Succinyl-CoA; xu5p-D, D-Xylulose 5-phosphate.

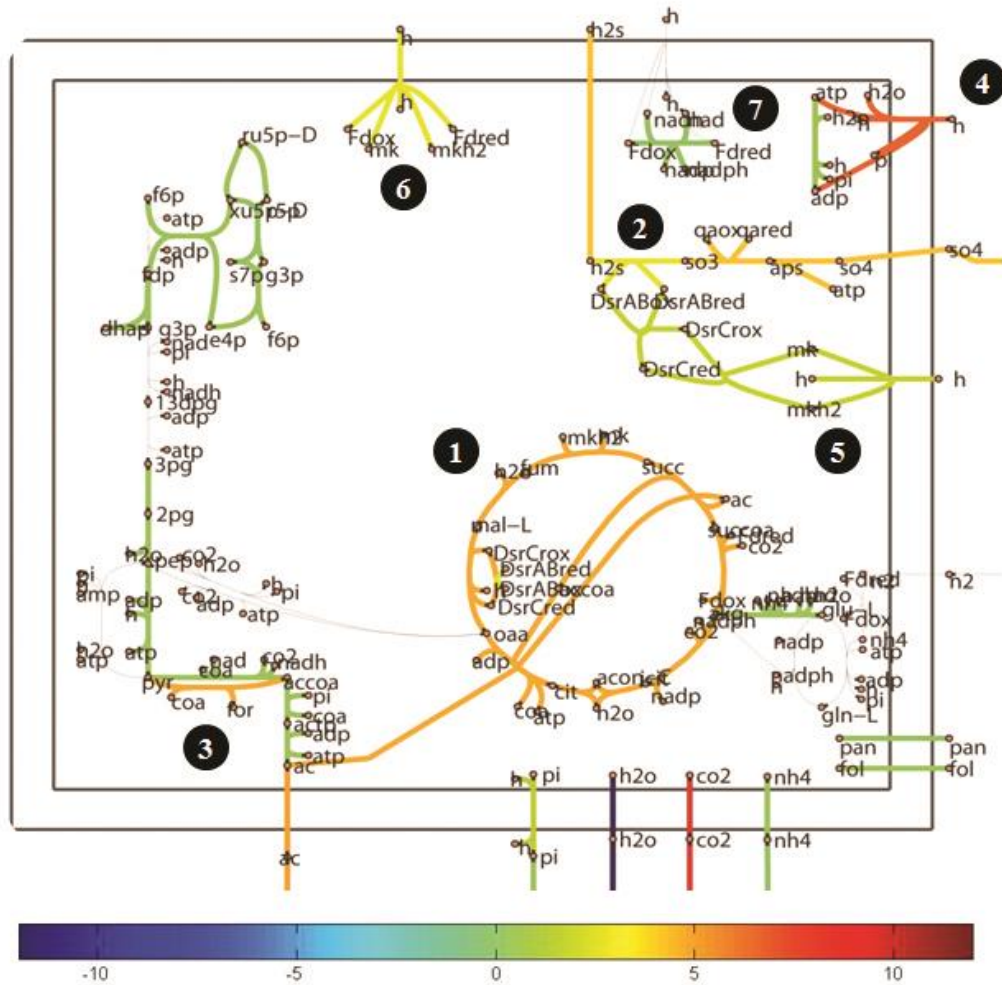


Figure C26: Representative portion of the metabolism of *D. postgatei* growing under electron donor limitation at  $0.032 \text{ h}^{-1}$ . The color of the line between metabolites indicates the flux rate for each reaction in  $\text{mmol/gdw h}$  (see numbers in color bar).

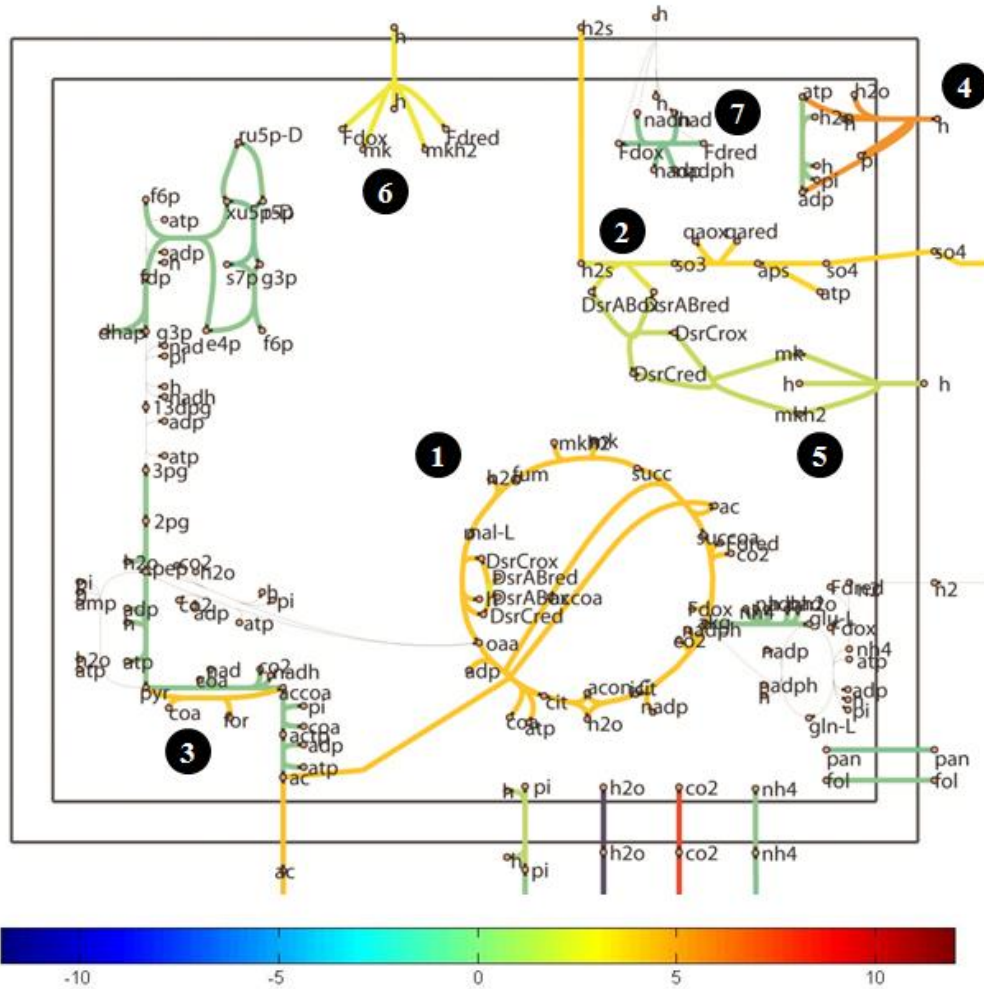


Figure C27: Representative portion of the metabolism of *D. postgatei* growing under electron donor limitation at  $0.028 \text{ h}^{-1}$ . The color of the line between metabolites indicates the flux rate for each reaction in  $\text{mmol/gdw h}$  (see numbers in color bar).



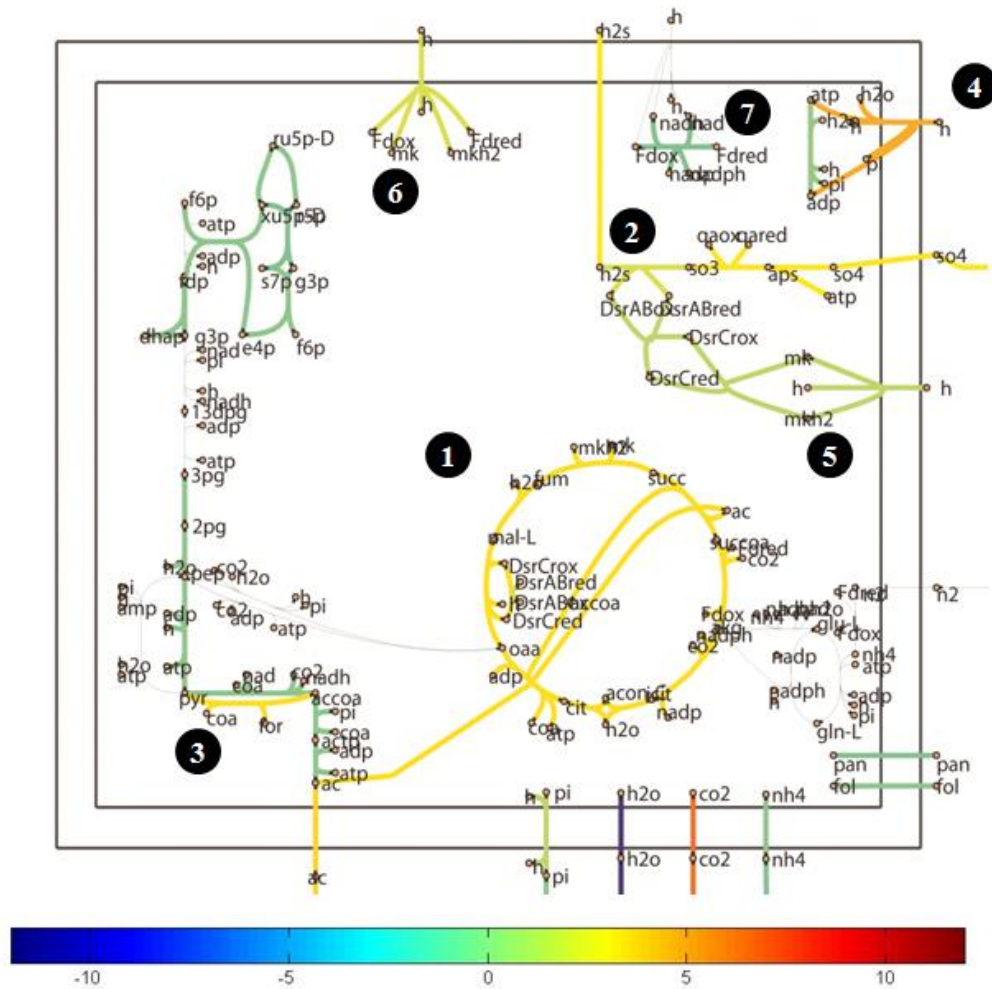


Figure C28: Representative portion of the metabolism of *D. postgatei* growing under electron donor limitation at  $0.024 \text{ h}^{-1}$ . The color of the line between metabolites indicates the flux rate for each reaction in mmol/gdw h (see numbers in color bar).

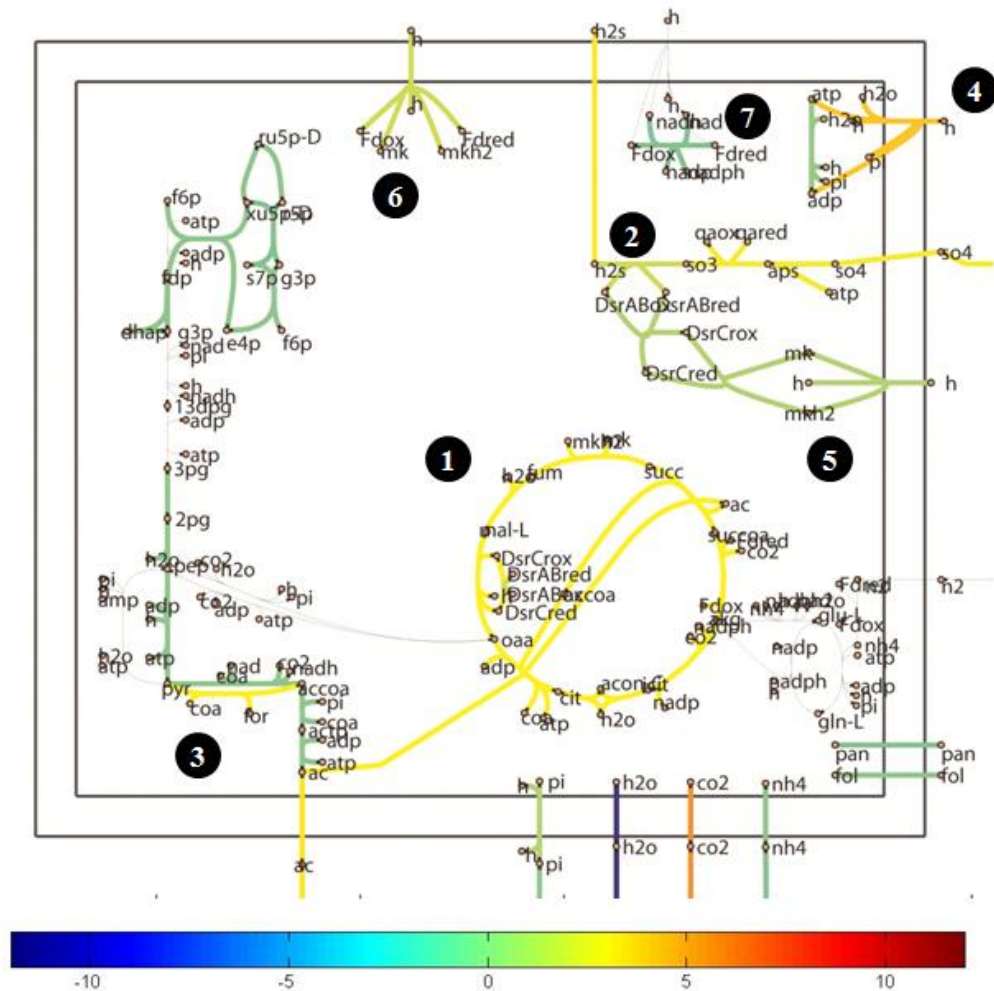


Figure C29: Representative portion of the metabolism of *D. postgatei* growing under electron donor limitation at  $0.021 \text{ h}^{-1}$ . The color of the line between metabolites indicates the flux rate for each reaction in mmol/gdw h (see numbers in color bar).

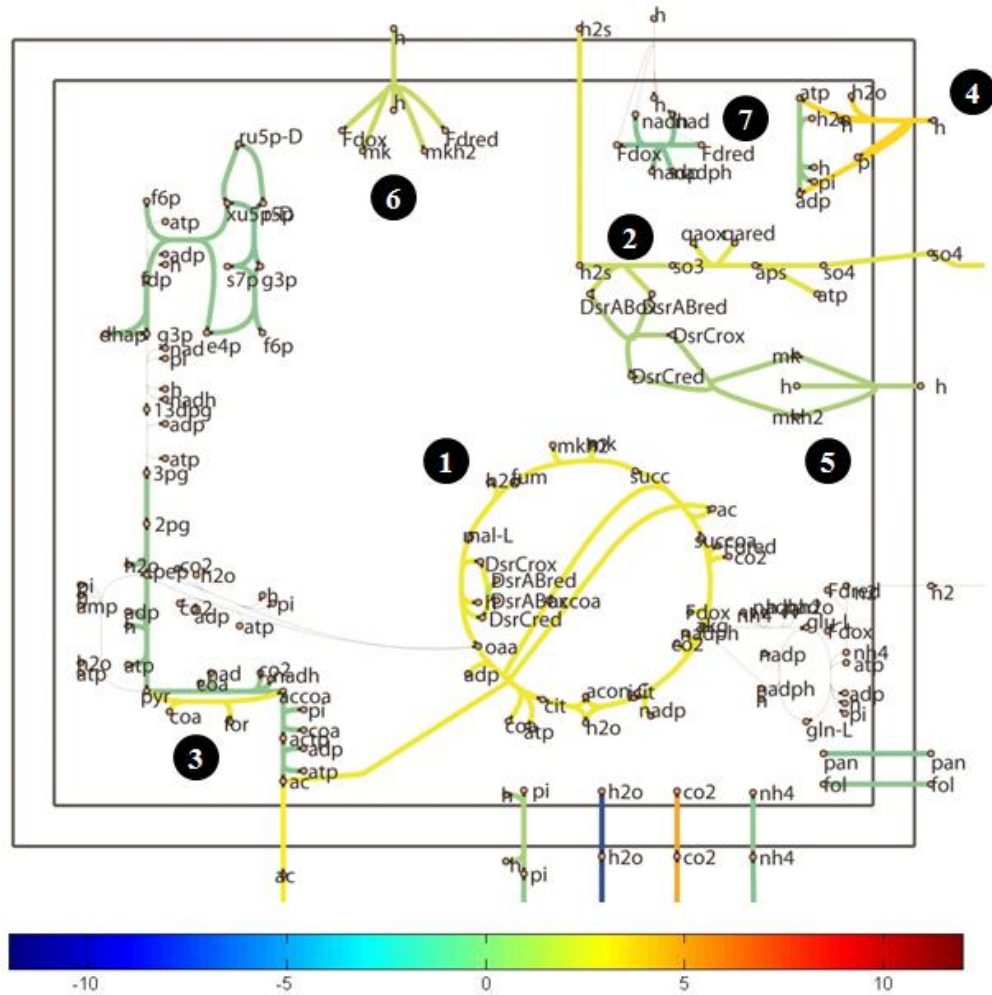


Figure C30: Representative portion of the metabolism of *D. postgatei* growing under electron donor limitation at  $0.017 \text{ h}^{-1}$ . The color of the line between metabolites indicates the flux rate for each reaction in mmol/gdw h (see numbers in color bar).

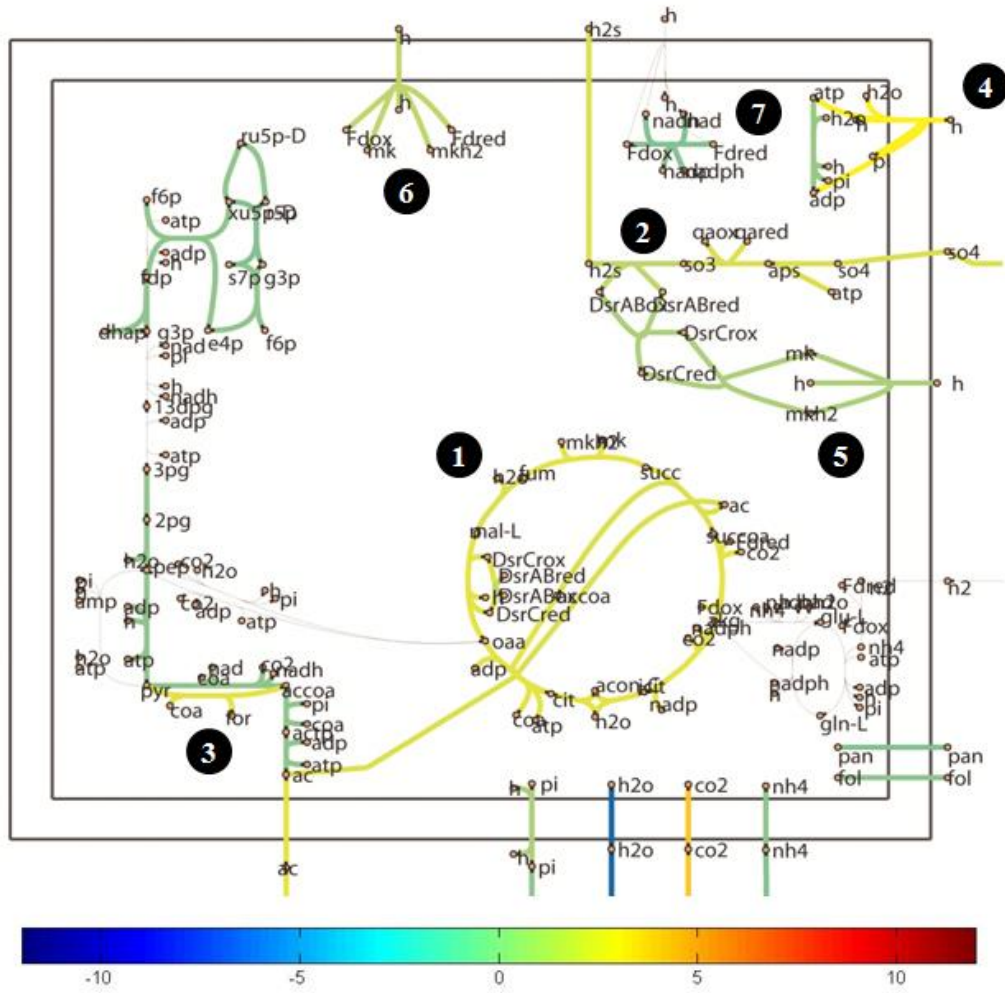


Figure C31: Representative portion of the metabolism of *D. postgatei* growing under electron donor limitation at  $0.014 \text{ h}^{-1}$ . The color of the line between metabolites indicates the flux rate for each reaction in mmol/gdw h (see numbers in color bar).

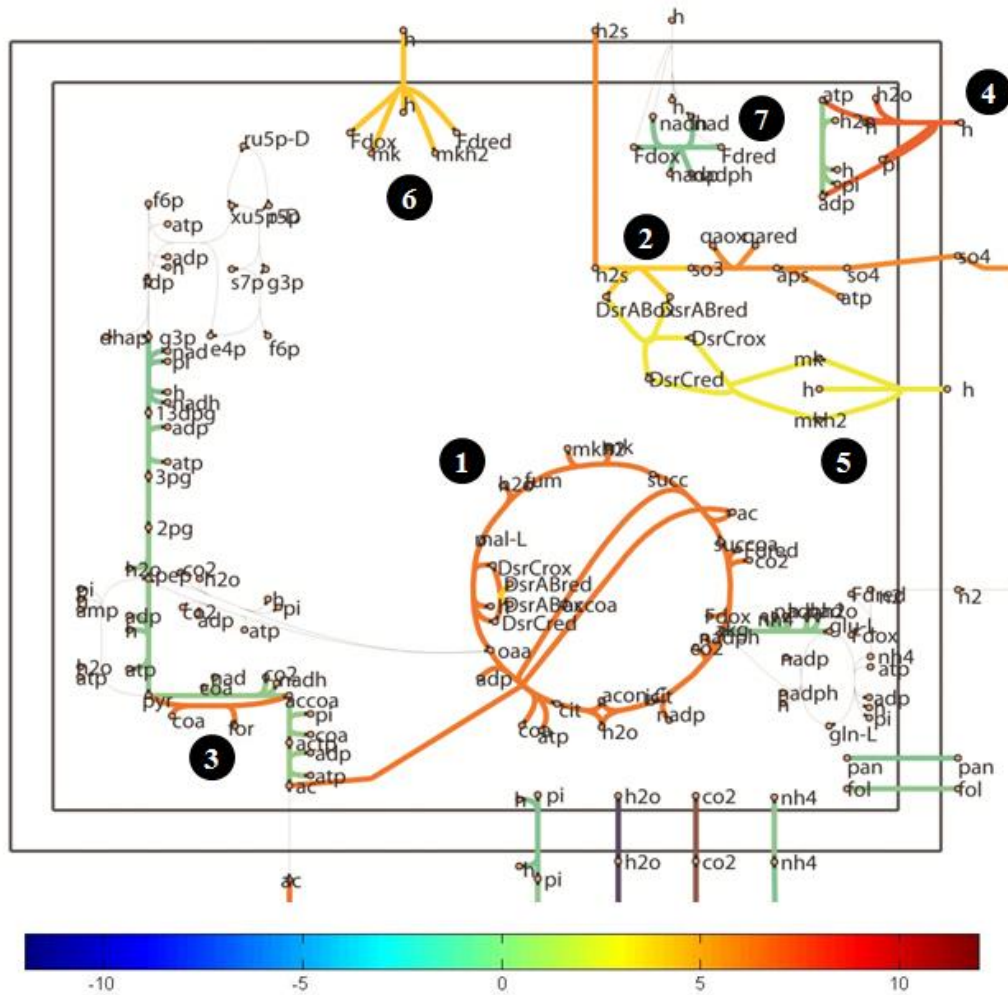


Figure C32: Representative portion of the metabolism of *D. postgatei* growing under electron acceptor limitation at  $0.032 \text{ h}^{-1}$ . The color of the line between metabolites indicates the flux rate for each reaction in mmol/gdw h (see numbers in color bar).

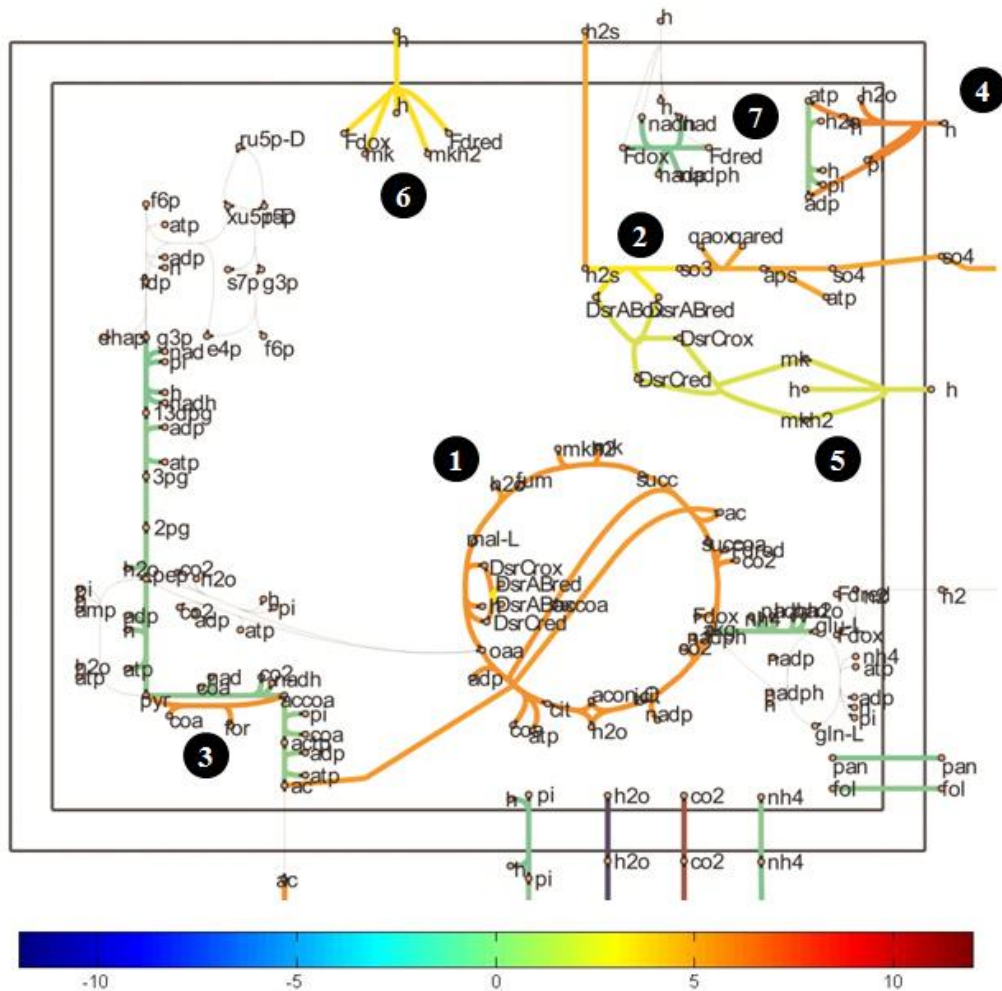


Figure C33: Representative portion of the metabolism of *D. postgatei* growing under electron acceptor limitation at  $0.028 \text{ h}^{-1}$ . The color of the line between metabolites indicates the flux rate for each reaction in mmol/gdw h (see numbers in color bar).



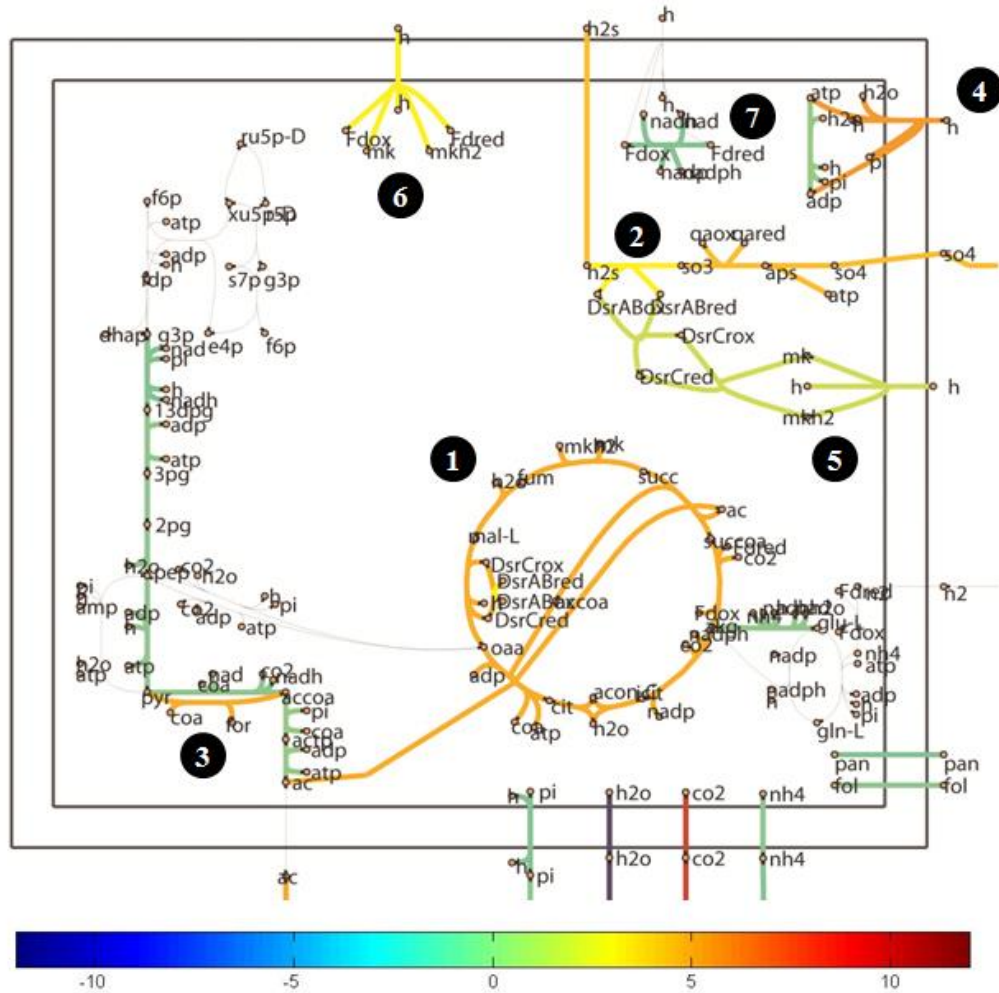


Figure C34: Representative portion of the metabolism of *D.postgatei* growing under electron acceptor limitation at  $0.024 \text{ h}^{-1}$ . The color of the line between metabolites indicates the flux rate for each reaction in  $\text{mmol/gdw h}$  (see numbers in color bar).

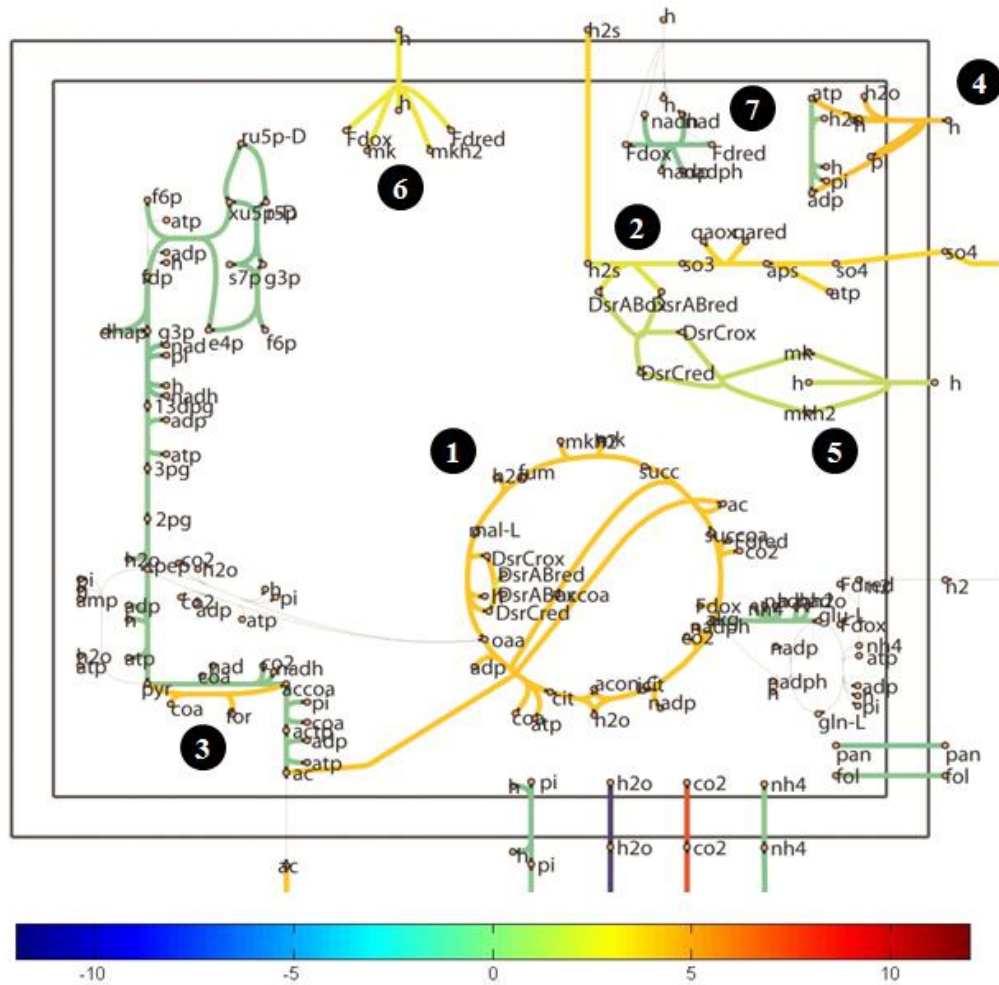


Figure C35: Representative portion of the metabolism of *D. postgatei* growing under electron acceptor limitation at  $0.021 \text{ h}^{-1}$ . The color of the line between metabolites indicates the flux rate for each reaction in mmol/gdw h (see numbers in color bar).



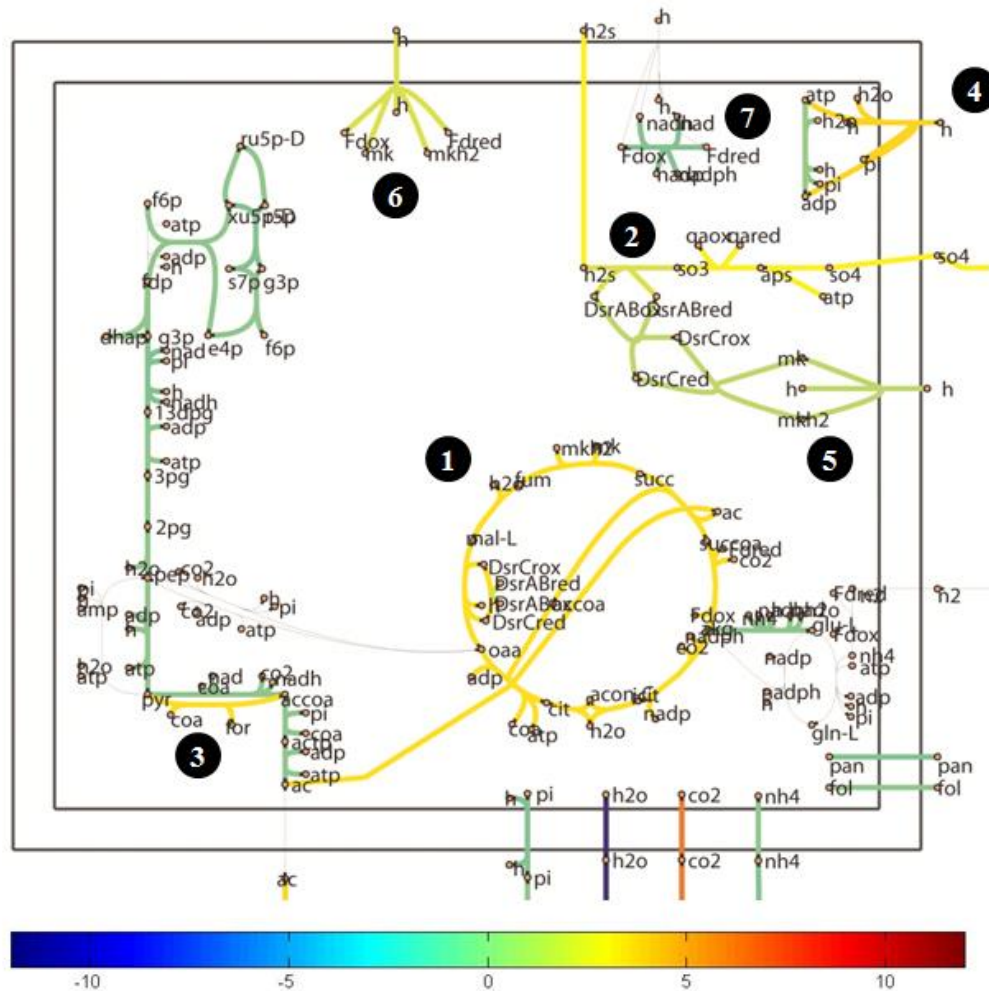


Figure C36: Representative portion of the metabolism of *D. postgatei* growing under electron acceptor limitation at  $0.017 \text{ h}^{-1}$ . The color of the line between metabolites indicates the flux rate for each reaction in  $\text{mmol/gdw h}$  (see numbers in color bar).

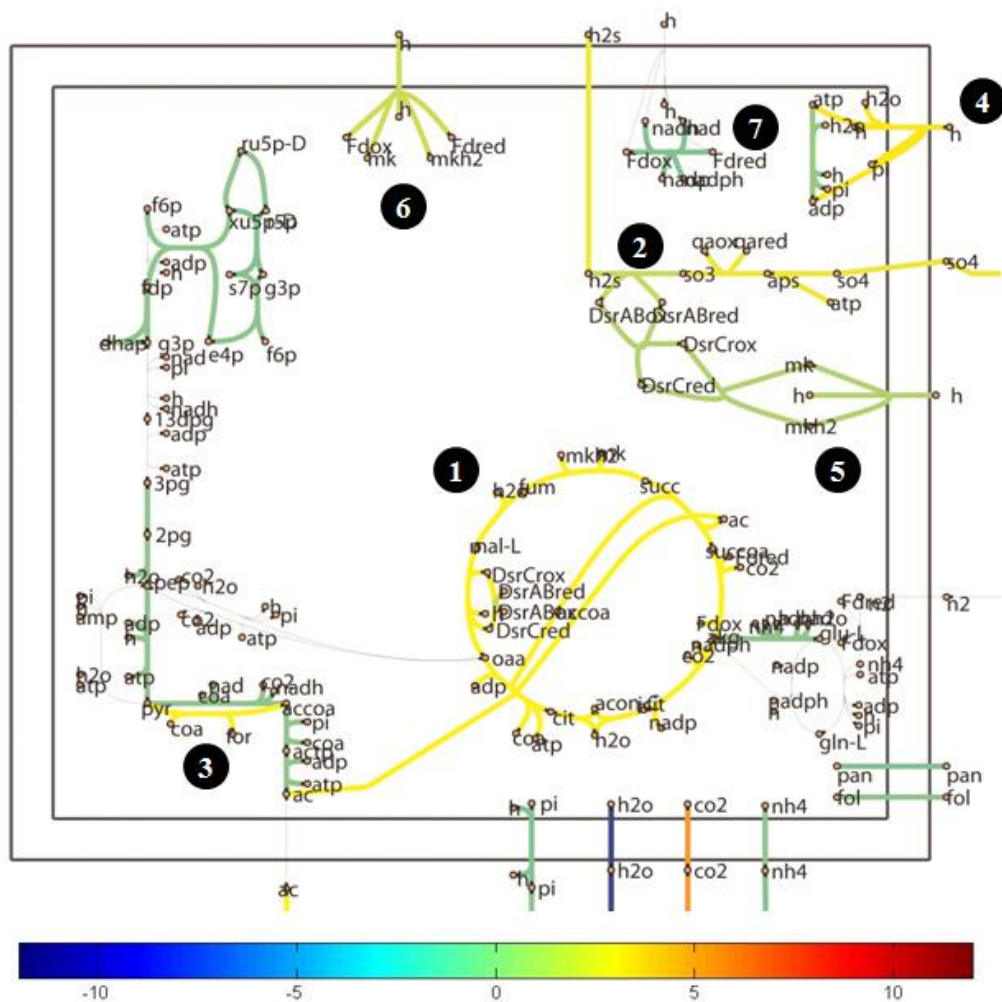


Figure C37: Representative portion of the metabolism of *D. postgatei* growing under electron acceptor limitation at  $0.014 \text{ h}^{-1}$ . The color of the line between metabolites indicates the flux rate for each reaction in  $\text{mmol/gdw h}$  (see numbers in color bar).

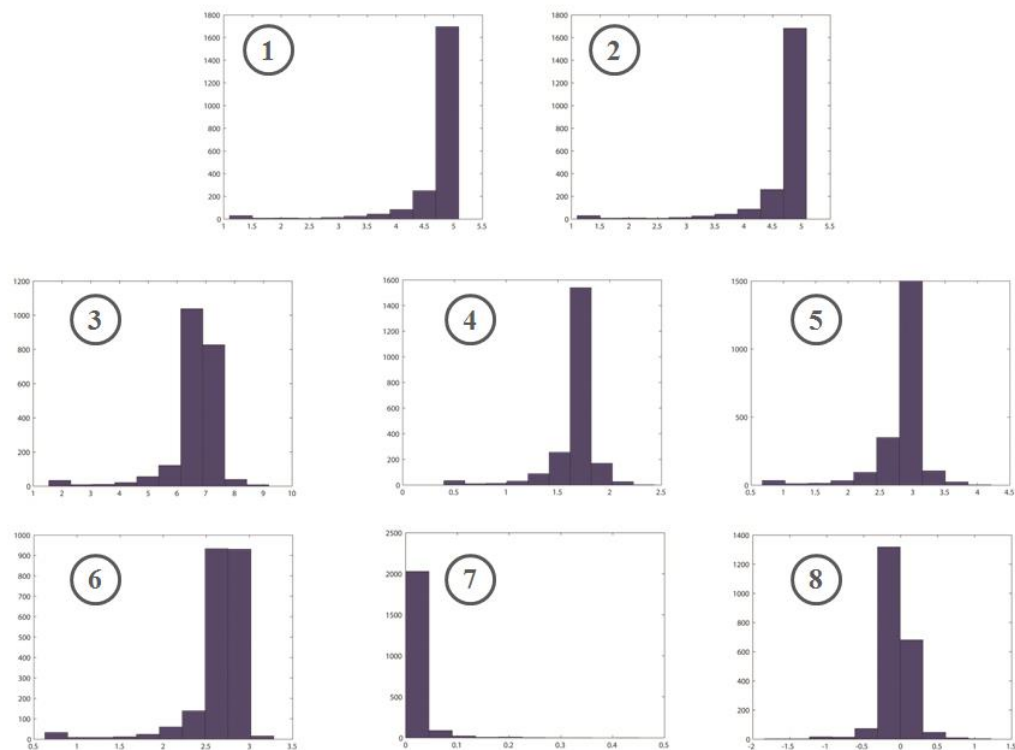


Figure C38: Probability flux distributions of *D.postgatei* growing under electron donor limitation at  $0.032 \text{ h}^{-1}$ . The *D.postgatei* metabolic model with imposed maximum and minimum constraints on each flux was sampled using the *in silico* Monte Carlo procedure. The histograms of each reaction represent the distribution of solutions (y-axis) with respect to each reaction flux (x-axis, in  $\text{mmol/gdw h}$ ). Reactions correspond as following: (1) ATP citrate lyase, (2) 2-oxoglutarate ferredoxin oxidoreductase, (3) ATP synthase, (4) Qrc complex, (5) Ferredoxin:menaquinone oxidoreductase, (6) Dissimilatory sulfite reductase, (7)  $\text{H}^+$ -translocating ferredoxin: $\text{NAD}^+$  oxidoreductase (Rnf), (8) NADH-dependent ferredoxin:NADP oxidoreductase (Nfn).

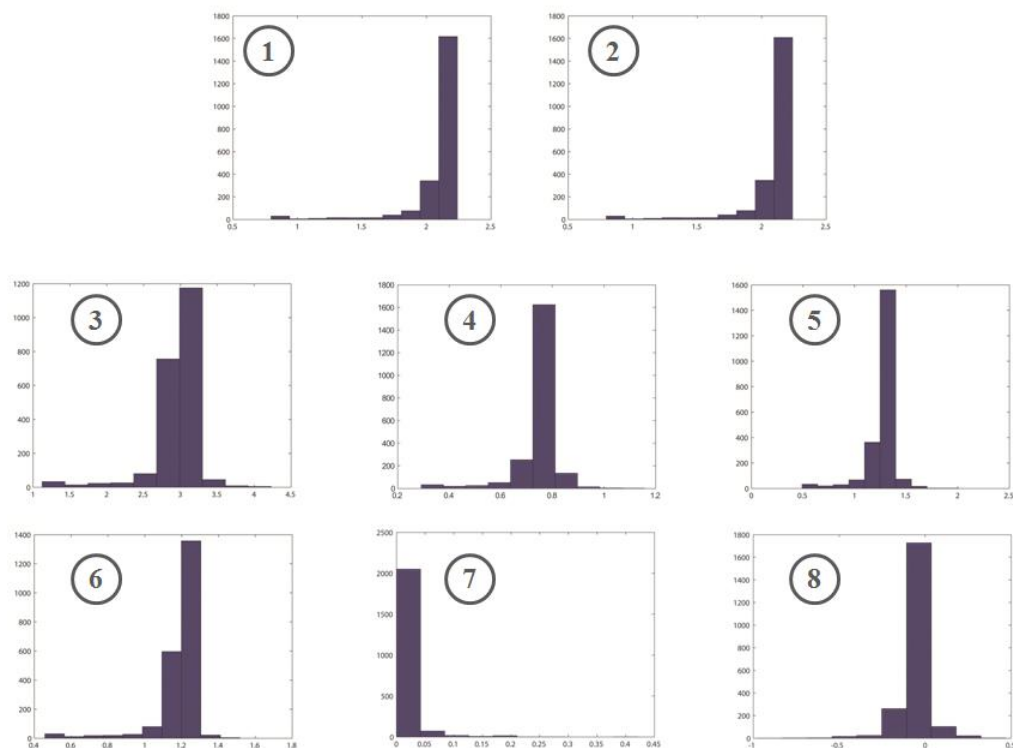


Figure C39: Probability flux distributions of *D.postgatei* growing under electron donor limitation at  $0.014 \text{ h}^{-1}$ . The *D.postgatei* metabolic model with imposed maximum and minimum constraints on each flux was sampled using the *in silico* Monte Carlo procedure. The histograms of each reaction represent the distribution of solutions (y-axis) with respect to each reaction flux (x-axis, in mmol/gdw h). Reactions correspond as following: (1) ATP citrate lyase, (2) 2-oxoglutarate ferredoxin oxidoreductase, (3) ATP synthase, (4) Qrc complex, (5) Ferredoxin:menaquinone oxidoreductase, (6) Dissimilatory sulfite reductase, (7) H<sup>+</sup>-translocating ferredoxin:NAD<sup>+</sup> oxidoreductase (Rnf), (8) NADH-dependent ferredoxin:NADP oxidoreductase (Nfn).

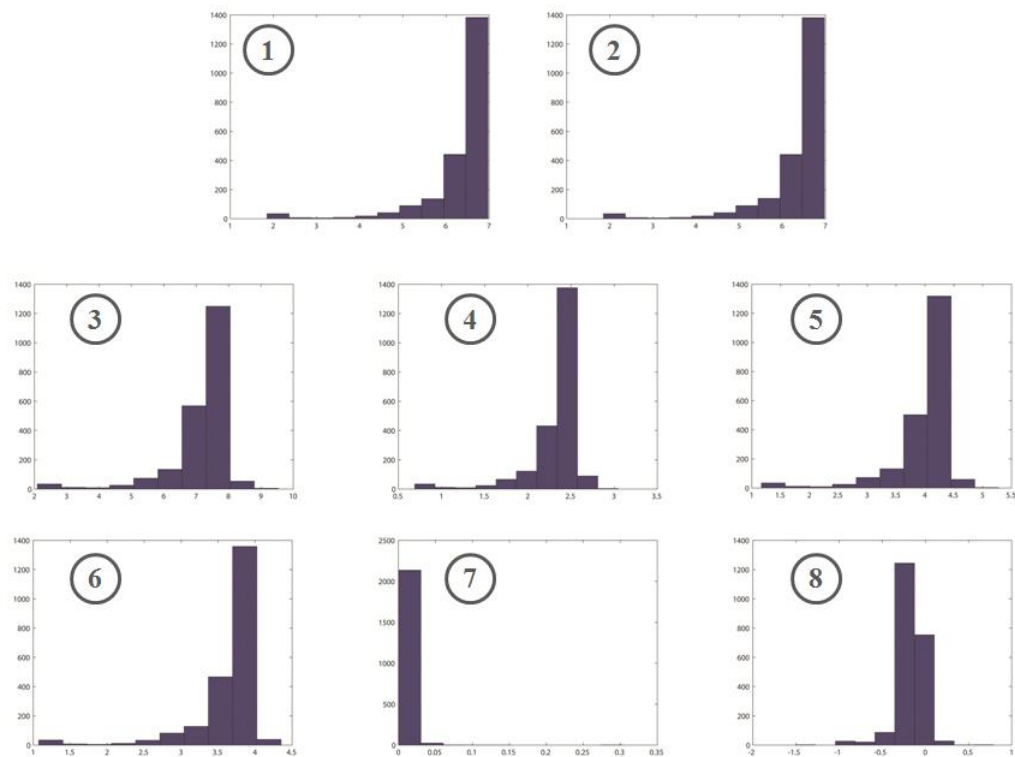


Figure C40: Probability flux distributions of *D.postgatei* growing under electron acceptor limitation at  $0.032 \text{ h}^{-1}$ . The *D.postgatei* metabolic model with imposed maximum and minimum constraints on each flux was sampled using the *in silico* Monte Carlo procedure. The histograms of each reaction represent the distribution of solutions (y-axis) with respect to each reaction flux (x-axis, in  $\text{mmol/gdw h}$ ). Reactions correspond as following: (1) ATP citrate lyase, (2) 2-oxoglutarate ferredoxin oxidoreductase, (3) ATP synthase, (4) Qrc complex, (5) Ferredoxin:menaquinone oxidoreductase, (6) Dissimilatory sulfite reductase, (7)  $\text{H}^+$ -translocating ferredoxin: $\text{NAD}^+$  oxidoreductase (Rnf), (8) NADH-dependent ferredoxin: $\text{NADP}$  oxidoreductase (Nfn).

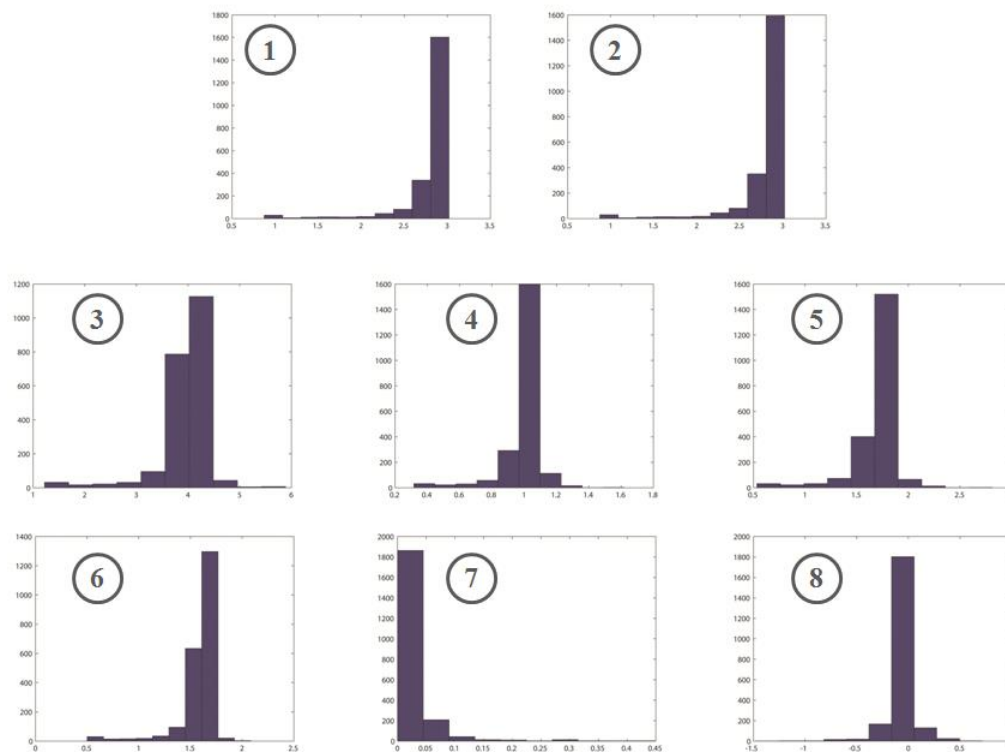


Figure C41: Probability flux distributions of *D.postgatei* growing under electron acceptor limitation at  $0.014 \text{ h}^{-1}$ . The *D.postgatei* metabolic model with imposed maximum and minimum constraints on each flux was sampled using the *in silico* Monte Carlo procedure. The histograms of each reaction represent the distribution of solutions (y-axis) with respect to each reaction flux (x-axis, in mmol/gdw h). Reactions correspond as following: (1) ATP citrate lyase, (2) 2-oxoglutarate ferredoxin oxidoreductase, (3) ATP synthase, (4) Qrc complex, (5) Ferredoxin:menaquinone oxidoreductase, (6) Dissimilatory sulfite reductase, (7) H<sup>+</sup>-translocating ferredoxin:NAD<sup>+</sup> oxidoreductase (Rnf), (8) NADH-dependent ferredoxin:NADP oxidoreductase (Nfn).

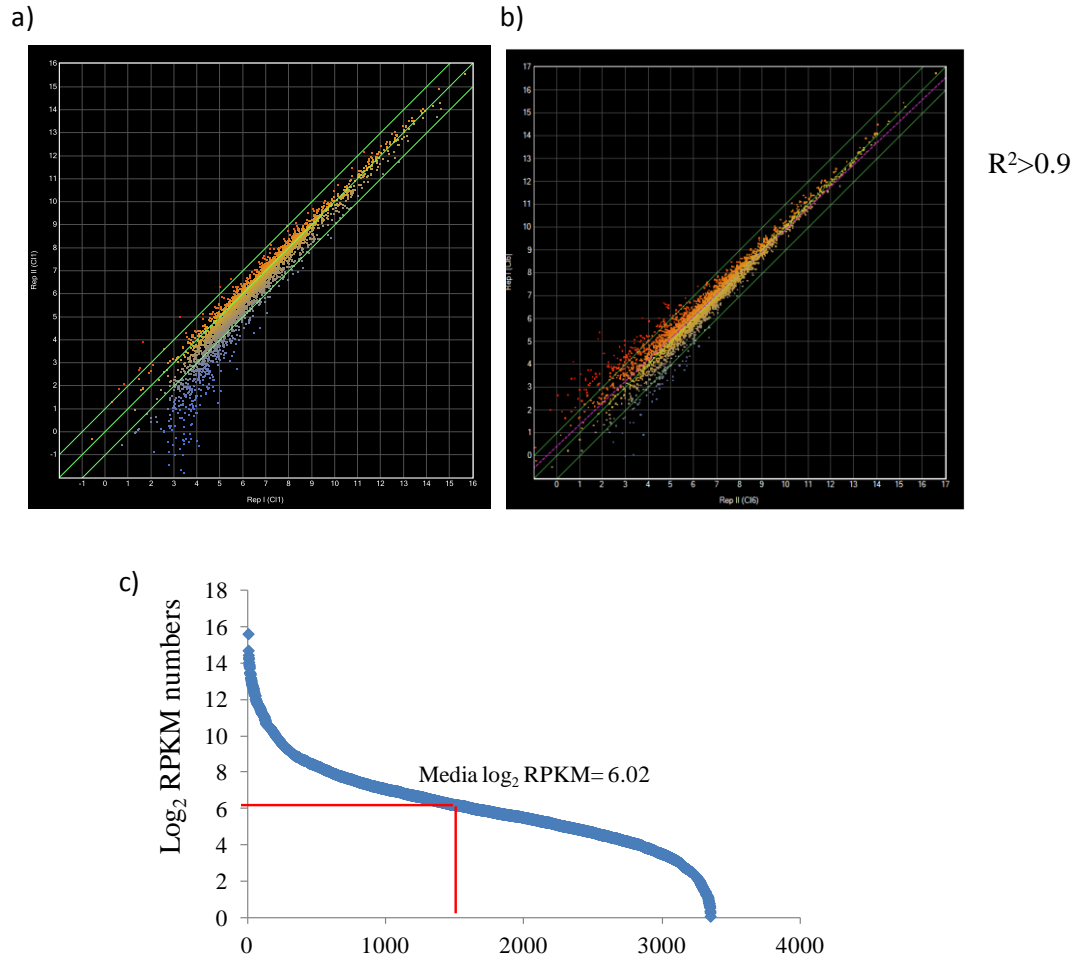


Figure C42 (a) Scatter plot showing comparison of gene expression levels in replicate culture of *D. postgatei* growing under electron donor (acetate) limitation at (a)0.032 h<sup>-1</sup> and (b)0.014 h<sup>-1</sup>. Each data point on the scatter plot represents an individual gene and is plotted based on its expression level in both of the selected experiments. Median log<sub>2</sub> RPKM value calculation. Only the gene expression levels above the median log<sub>2</sub> RPKM values were treated as the significant expression.

Table C18: Genes that were differentially expressed at least two fold in *D. postgatei* growing at 0.032 h<sup>-1</sup> compared to those growing at 0.014 h<sup>-1</sup> (P-value cutoff less than or equal to 0.05). Positive and negative numbers indicate up- and down-regulated genes at 0.032 h<sup>-1</sup>.

| <b>Locus tag</b> | <b>Function</b>  | <b>Fold change</b> | <b>P value</b> |
|------------------|--|--------------------|----------------|
| DespoDRAFT_00001 | hypothetical protein   | -1.457             | 0.431          |
| DespoDRAFT_00002 | hypothetical protein   | -1.505             | 0.608          |
| DespoDRAFT_00003 | hypothetical protein   | -1.51              | 0.586          |
| DespoDRAFT_00009 | transcriptional regulator  | 1.145              | 0.103          |
| DespoDRAFT_00011 | hypothetical protein   | -6.588             | 0.24           |
| DespoDRAFT_00014 | hypothetical protein   | 1.708              | 0.36           |
| DespoDRAFT_00020 | hypothetical protein   | -1.488             | 0.28           |
| DespoDRAFT_00023 | putative addiction module killer protein   | -1.349             | 0.502          |
| DespoDRAFT_00024 | putative addiction module antidote protein   | -1.914             | 0.0557         |
| DespoDRAFT_00028 | transcriptional regulator containing GAF, AAA-type ATPase, and DNA binding domains   | 1.197              | 0.336          |
| DespoDRAFT_00031 | hypothetical protein   | -1.522             | 0.472          |
| DespoDRAFT_00032 | HD superfamily phosphohydrolase  | 1.485              | 0.498          |
| DespoDRAFT_00033 | hypothetical protein   | -3.654             | 0.383          |
| DespoDRAFT_00034 | glyceraldehyde-3-phosphate dehydrogenase/erythrose-4-phosphate dehydrogenase         | -1.483             | 0.119          |
| DespoDRAFT_00035 | Pyruvate kinase  | -1.411             | 0.112          |
| DespoDRAFT_00036 | hypothetical protein   | -1.243             | 0.16           |
| DespoDRAFT_00037 | Pyruvate kinase  | -1.195             | 0.783          |
| DespoDRAFT_00038 | hypothetical protein   | 1.199              | 0.766          |
| DespoDRAFT_00039 | putative permease  | 1.059              | 0.95           |
| DespoDRAFT_00040 | response regulator with CheY-like receiver, AAA-type ATPase, and DNA-binding domains | -3.349             | 0.0957         |
| DespoDRAFT_00041 | vitamin B12 dependent methionine synthase  | -1.065             | 0.611          |
| DespoDRAFT_00042 | Homocysteine S-methyltransferase   | 1.207              | 0.16           |
| DespoDRAFT_00043 | hypothetical protein   | -1.386             | 0.679          |
| DespoDRAFT_00044 | signal transduction histidine kinase   | -2.14              | 0.187          |
| DespoDRAFT_00045 | diguanylate cyclase (GGDEF) domain-containing protein                                | -1.922             | 0.095          |
| DespoDRAFT_00048 | hypothetical protein   | -1.416             | NaN            |
| DespoDRAFT_00049 | glycogen synthase  | -1.402             | 0.27           |
| DespoDRAFT_00050 | ADP-ribose pyrophosphatase   | -1.496             | 0.0743         |
| DespoDRAFT_00054 | cobalamin biosynthesis protein CbiK, Co <sup>2+</sup> chelatase                      | -1.002             | 0.994          |



|                  |  |         |         |
|------------------|--|---------|---------|
| DespoDRAFT_00055 | putative metal-binding protein                               | 1.153   | 0.616   |
| DespoDRAFT_00056 | putative phosphohydrolase                                    | -1.312  | 0.287   |
| DespoDRAFT_00057 | P-type ATPase, translocating                                 | 1.087   | 0.688   |
| DespoDRAFT_00058 | hypothetical protein   | 1.978   | 0.344   |
| DespoDRAFT_00059 | putative domain HDIG-containing protein                      | -1.149  | 0.565   |
| DespoDRAFT_00060 | peptide chain release factor 2                               | -1.142  | 0.359   |
| DespoDRAFT_00061 | apolipoprotein N-acyltransferase                             | 1.361   | 0.557   |
| DespoDRAFT_00062 | Response regulator receiver domain protein, histidine kinase | -2.166  | 0.317   |
| DespoDRAFT_00063 | molecular chaperone (small heat shock protein)               | -1.226  | 0.861   |
| DespoDRAFT_00064 | ATP-dependent protease La                                    | -1.52   | 0.294   |
| DespoDRAFT_00065 | rare lipoprotein A   | -1.164  | 0.721   |
| DespoDRAFT_00066 | histidinol-phosphate phosphatase family protein              | 1.063   | 0.875   |
| DespoDRAFT_00067 | helicase, putative, RecD/TraA family                         | 1.186   | 0.759   |
| DespoDRAFT_00068 | hypothetical protein   | 1.344   | 0.334   |
| DespoDRAFT_00069 | hypothetical protein   | #VALUE! | NaN     |
| DespoDRAFT_00070 | transcription termination factor                             | 1.752   | 0.126   |
| DespoDRAFT_00071 | ATP-dependent protease La                                    | 1.292   | 0.09    |
| DespoDRAFT_00072 | endopeptidase Clp ATP-binding regulatory subunit ClpX        | -1.071  | 0.553   |
| DespoDRAFT_00073 | ATP-dependent Clp protease, proteolytic subunit ClpP         | -1.354  | 0.0359  |
| DespoDRAFT_00074 | trigger factor   | 2.275   | 0.00431 |
| DespoDRAFT_00076 | site-specific recombinase XerD                               | 1.101   | 0.949   |
| DespoDRAFT_00077 | TraX protein   | -2.368  | 0.574   |
| DespoDRAFT_00078 | hypothetical protein   | -1.275  | NaN     |
| DespoDRAFT_00079 | hypothetical protein   | 1.038   | 0.985   |
| DespoDRAFT_00080 | hypothetical protein   | #VALUE! | NaN     |
| DespoDRAFT_00081 | hypothetical protein   | -1.499  | 0.456   |
| DespoDRAFT_00082 | hypothetical protein   | -2.889  | 0.0827  |
| DespoDRAFT_00085 | hypothetical protein   | -1.249  | 0.616   |
| DespoDRAFT_00086 | zonula occludens toxin                                       | 1.544   | NaN     |
| DespoDRAFT_00087 | Protein of unknown function (DUF2523)                        | #VALUE! | NaN     |
| DespoDRAFT_00088 | hypothetical protein   | -5.315  | 0.48    |
| DespoDRAFT_00089 | hypothetical protein   | -3.603  | 0.336   |
| DespoDRAFT_00090 | hypothetical protein   | -1.92   | 0.664   |
| DespoDRAFT_00091 | hypothetical protein   | #VALUE! | NaN     |
| DespoDRAFT_00092 | hypothetical protein   | -1.743  | NaN     |
| DespoDRAFT_00093 | Helix-turn-helix protein                                     | 1.198   | 0.751   |
| DespoDRAFT_00094 | hypothetical protein   | 1.516   | 0.701   |
| DespoDRAFT_00095 | hypothetical protein   | -1.451  | 0.494   |
| DespoDRAFT_00096 | hypothetical protein   | -1.849  | 0.127   |
| DespoDRAFT_00097 | hypothetical protein   | -1.871  | 0.123   |

|                  |   |        |        |
|------------------|---|--------|--------|
| DespoDRAFT_00098 | hypothetical protein  | -1.09  | 0.942  |
| DespoDRAFT_00099 | hypothetical protein  | -2.627 | 0.156  |
| DespoDRAFT_00100 | phosphate ABC transporter, phosphate-binding protein                                    | 6.279  | 0.0556 |
| DespoDRAFT_00101 | phosphate ABC transporter, permease protein PstC  | -1.11  | 0.691  |
| DespoDRAFT_00102 | phosphate ABC transporter, permease protein PstA  | -1.183 | 0.834  |
| DespoDRAFT_00103 | phosphate ABC transporter, ATP-binding protein  | -1.204 | 0.384  |
| DespoDRAFT_00104 | Phosphoenolpyruvate carboxylase   | 1.167  | 0.785  |
| DespoDRAFT_00105 | hypothetical protein  | 1.556  | 0.177  |
| DespoDRAFT_00106 | 2-oxoacid:acceptor oxidoreductase, delta subunit  | 2.619  | 0.0138 |
| DespoDRAFT_00107 | 2-Oxoglutarate:ferredoxin oxidoreductase a subunit                                      | 2.721  | 0.053  |
| DespoDRAFT_00108 | 2-Oxoglutarate:ferredoxin oxidoreductase b subunit                                      | 2.829  | 0.0723 |
| DespoDRAFT_00109 | 2-oxoacid:acceptor oxidoreductase, gamma subunit; pyruvate/2-ketoisovalerate family     | 2.156  | 0.0523 |
| DespoDRAFT_00110 | acyl-CoA dehydrogenase  | 3.476  | 0.0347 |
| DespoDRAFT_00111 | putative transcriptional regulator with cupin domain                                    | 4.09   | 0.06   |
| DespoDRAFT_00112 | branched-chain amino acid aminotransferase, group II                                    | 5.158  | 0.0325 |
| DespoDRAFT_00113 | radical SAM domain iron- sulfur cluster-binding oxidoreductase                          | 1.961  | 0.177  |
| DespoDRAFT_00114 | metal-dependent hydrolase   | -1.558 | 0.267  |
| DespoDRAFT_00115 | response regulator containing a CheY-like receiver domain and an HTH DNA-binding domain | -1.416 | 0.0587 |
| DespoDRAFT_00116 | hypothetical protein  | -1.453 | 0.21   |
| DespoDRAFT_00117 | hypothetical protein  | -1.594 | 0.0676 |
| DespoDRAFT_00118 | membrane-bound serine protease (ClpP class)   | -5.071 | 0.254  |
| DespoDRAFT_00119 | membrane-bound serine protease (ClpP class)   | -1.838 | 0.116  |
| DespoDRAFT_00120 | Mn-dependent transcriptional regulator  | -3.113 | 0.0344 |
| DespoDRAFT_00121 | putative DNA-binding protein  | -2.943 | 0.0586 |
| DespoDRAFT_00122 | histidinol dehydrogenase  | 1.321  | 0.276  |
| DespoDRAFT_00124 | hypothetical protein  | 1.017  | 0.987  |
| DespoDRAFT_00126 | ATP synthase, F1 beta subunit   | -3.213 | 0.103  |
| DespoDRAFT_00127 | alternate F1F0 ATPase, F1 subunit epsilon   | -2.338 | 0.0229 |
| DespoDRAFT_00128 | ATP synthase, F0F1 subunit  | -3.234 | 0.0509 |
| DespoDRAFT_00129 | F1/F0 ATPase,subunit 2  | -3.062 | 0.433  |

|                  |   |         |        |
|------------------|---|---------|--------|
| DespoDRAFT_00130 | ATP synthase, F0 Alpha subunit  | -1.608  | 0.387  |
| DespoDRAFT_00131 | ATP synthase, F0 subunit c  | -4.885  | 0.227  |
| DespoDRAFT_00132 | F0F1-type ATP synthase, beta subunit  | -2.798  | 0.0951 |
| DespoDRAFT_00133 | ATP synthase, F1 beta subunit   | -2.51   | 0.0925 |
| DespoDRAFT_00134 | ATP synthase, F1 beta subunit   | -3.488  | 0.181  |
| DespoDRAFT_00135 | hypothetical protein  | -1.069  | 0.936  |
| DespoDRAFT_00136 | apurinic endonuclease APN1  | 3.373   | 0.21   |
| DespoDRAFT_00137 | putative efflux protein, MATE family  | 2.231   | 0.664  |
| DespoDRAFT_00138 | nicotinate-nucleotide--<br>dimethylbenzimidazole<br>phosphoribosyltransferase                 | 4.643   | 0.225  |
| DespoDRAFT_00139 | DNA/RNA helicase, superfamily II  | -1.064  | 0.663  |
| DespoDRAFT_00140 | hydrogenase assembly chaperone<br>HypC/HupF   | -1.422  | 0.442  |
| DespoDRAFT_00141 | (NiFe) hydrogenase maturation protein<br>HypF   | -1.261  | 0.766  |
| DespoDRAFT_00142 | hydrogenase expression/formation protein<br>HypD  | #VALUE! | 1      |
| DespoDRAFT_00143 | hydrogenase expression/formation protein<br>HypE  | 1.198   | 0.221  |
| DespoDRAFT_00144 | RNA polymerase-binding protein DksA   | -1.872  | 0.106  |
| DespoDRAFT_00145 | ribonuclease III  | -1.154  | 0.103  |
| DespoDRAFT_00146 | histone acetyltransferase   | 1.796   | 0.148  |
| DespoDRAFT_00147 | 2' 5' RNA ligase family protein   | -1.8    | 0.501  |
| DespoDRAFT_00148 | putative polymerase with PALM domain,<br>HD hydrolase domain and Zn ribbon                    | -1.303  | 0.498  |
| DespoDRAFT_00151 | hypothetical protein  | 1.664   | 0.108  |
| DespoDRAFT_00152 | ATP:corrinoid adenosyltransferase   | 1.723   | 0.103  |
| DespoDRAFT_00153 | ATP citrate lyase alpha subunit (AclA)  | 1.191   | 0.262  |
| DespoDRAFT_00154 | ATP citrate lyase beta subunit (AclB)   | 1.098   | 0.426  |
| DespoDRAFT_00155 | hypothetical protein  | -1.3    | 0.458  |
| DespoDRAFT_00156 | histidyl-tRNA synthetase  | 2.936   | 0.0592 |
| DespoDRAFT_00157 | aspartyl-tRNA synthetase  | 2.694   | 0.0365 |
| DespoDRAFT_00158 | cell division topological specificity factor<br>MinE  | -1.162  | 0.282  |
| DespoDRAFT_00159 | septum site-determining protein MinD  | 1.086   | 0.331  |
| DespoDRAFT_00160 | septum formation inhibitor  | -1.233  | 0.0497 |
| DespoDRAFT_00161 | histidine kinase, Response regulator<br>receiver domain protein, histidine kinase             | -2.029  | 0.0676 |
| DespoDRAFT_00162 | response regulator containing a CheY-like<br>receiver domain and an HTH DNA-binding<br>domain | -1.776  | 0.176  |
| DespoDRAFT_00163 | 3-dehydroquinate synthase   | 1.079   | 0.585  |
| DespoDRAFT_00164 | rubrerythrin  | -1.219  | 0.507  |
| DespoDRAFT_00165 | thioredoxin   | 1.059   | 0.733  |

|                  |   |        |        |
|------------------|---|--------|--------|
| DespoDRAFT_00166 | thioredoxin-disulfide reductase   | -1.107 | 0.143  |
| DespoDRAFT_00167 | outer membrane assembly lipoprotein YfiO  | 1.009  | 0.952  |
| DespoDRAFT_00168 | ribosomal protein L28   | 1.375  | 0.458  |
| DespoDRAFT_00169 | PhoH family protein   | 1.248  | 0.778  |
| DespoDRAFT_00170 | (p)ppGpp synthetase, RelA/SpoT family   | 1.101  | 0.755  |
| DespoDRAFT_00171 | prolyl-tRNA synthetase, family I  | -1.179 | 0.0185 |
| DespoDRAFT_00172 | 1-hydroxy-2-methyl-2-(E)-butenyl 4-diphosphate synthase                               | -1.117 | 0.0635 |
| DespoDRAFT_00173 | type I restriction-modification system methyltransferase subunit                      | -1.018 | 0.959  |
| DespoDRAFT_00174 | hypothetical protein  | 1.309  | 0.774  |
| DespoDRAFT_00175 | restriction endonuclease S subunit  | -1.74  | 0.763  |
| DespoDRAFT_00177 | DnaJ-class molecular chaperone with C-terminal Zn finger domain                       | -2.325 | 0.146  |
| DespoDRAFT_00178 | hypothetical protein  | -1.656 | NaN    |
| DespoDRAFT_00179 | molecular chaperone (small heat shock protein)  | -4.425 | 0.383  |
| DespoDRAFT_00181 | aconitase A   | 2.552  | 0.0261 |
| DespoDRAFT_00182 | putative permease   | 2.219  | 0.583  |
| DespoDRAFT_00183 | saccharopine dehydrogenase-like oxidoreductase  | -1.393 | 0.482  |
| DespoDRAFT_00184 | glucokinase   | 1.137  | 0.935  |
| DespoDRAFT_00185 | methylase involved in ubiquinone/menaquinone biosynthesis                             | -1.035 | 0.965  |
| DespoDRAFT_00186 | D-alanine aminotransferase  | 1.286  | 0.315  |
| DespoDRAFT_00187 | alanine racemase  | 1.31   | 0.386  |
| DespoDRAFT_00189 | hypothetical protein  | 1.043  | 0.972  |
| DespoDRAFT_00192 | hypothetical protein  | -1.437 | 0.128  |
| DespoDRAFT_00193 | acetyl-CoA hydrolase  | -1.2   | 0.557  |
| DespoDRAFT_00194 | hypothetical protein  | -1.261 | 0.203  |
| DespoDRAFT_00195 | Protein of unknown function (DUF2914)   | -1.225 | 0.862  |
| DespoDRAFT_00196 | hypothetical protein  | 1.044  | 0.986  |
| DespoDRAFT_00197 | putative Acetyl-CoA synthetase  | -1.53  | 0.221  |
| DespoDRAFT_00198 | hypothetical protein  | -1.295 | 0.345  |
| DespoDRAFT_00199 | membrane-associated lipoprotein involved in thiamine biosynthesis                     | 1.067  | 0.782  |
| DespoDRAFT_00200 | Pyridoxamine 5''-phosphate oxidase  | -1.291 | 0.21   |
| DespoDRAFT_00201 | PAS domain S-box  | 1.138  | 0.897  |
| DespoDRAFT_00202 | response regulator with CheY-like receiver domain and winged-helix DNA-binding domain | -1.419 | 0.381  |
| DespoDRAFT_00203 | 2-oxoacid:ferredoxin oxidoreductase, gamma subunit                                    | 3.301  | 0.0149 |
| DespoDRAFT_00204 | 2-Oxoglutarate:ferredoxin oxidoreductase beta subunit                                 | 3.356  | 0.0463 |

|                  |   |         |        |
|------------------|---|---------|--------|
| DespoDRAFT_00205 | 2-oxoglutarate ferredoxin oxidoreductase subunit alpha                                    | 3.648   | 0.0274 |
| DespoDRAFT_00206 | ferredoxin  | 3.876   | 0.0458 |
| DespoDRAFT_00207 | glycosyl transferase  | -1.056  | 0.748  |
| DespoDRAFT_00208 | beta-lactamase domain protein   | -1.102  | 0.651  |
| DespoDRAFT_00210 | glycyl-tRNA synthetase, dimeric type  | -1.516  | 0.218  |
| DespoDRAFT_00211 | isoleucine patch superfamily enzyme, carbonic anhydrase/acetyltransferase                 | 1.981   | 0.108  |
| DespoDRAFT_00212 | heterodisulfide reductase, subunit B  | 2.164   | 0.137  |
| DespoDRAFT_00213 | hypothetical protein  | 1.956   | 0.0254 |
| DespoDRAFT_00214 | citrate lyase beta subunit  | -1.635  | 0.128  |
| DespoDRAFT_00215 | dihydrolipoamide dehydrogenase  | -2.195  | 0.101  |
| DespoDRAFT_00216 | lipoate-protein ligase A  | -1.767  | 0.181  |
| DespoDRAFT_00217 | phosphopantetheine-containing protein   | -2.802  | 0.108  |
| DespoDRAFT_00218 | pyruvate/2-oxoglutarate dehydrogenase complex, dihydrolipoamide acyltransferase component | -2.637  | 0.173  |
| DespoDRAFT_00219 | pyruvate/2-oxoglutarate dehydrogenase complex, dehydrogenase component beta subunit       | -3.73   | 0.105  |
| DespoDRAFT_00220 | pyruvate dehydrogenase E1 component, alpha subunit  | -3.077  | 0.029  |
| DespoDRAFT_00221 | acetyl-CoA synthetase   | -2.402  | 0.237  |
| DespoDRAFT_00222 | hypothetical protein  | 1.25    | 0.794  |
| DespoDRAFT_00224 | P-type ATPase, translocating  | -1.056  | 0.661  |
| DespoDRAFT_00227 | hypothetical protein  | #VALUE! | NaN    |
| DespoDRAFT_00228 | diguanylate cyclase (GGDEF) domain-containing protein                                     | -3.113  | 0.122  |
| DespoDRAFT_00229 | micrococcal nuclease-like nuclease  | -1.987  | 0.0556 |
| DespoDRAFT_00230 | ribosomal protein L11 methylase   | 1.436   | 0.478  |
| DespoDRAFT_00231 | hypothetical protein  | 1.966   | 0.0801 |
| DespoDRAFT_00232 | Uncharacterized protein family (UPF0153)  | 2.174   | 0.0729 |
| DespoDRAFT_00233 | tRNA modification GTPase TrmE   | 1.568   | 0.109  |
| DespoDRAFT_00234 | putative RNA-binding protein  | 1.146   | 0.651  |
| DespoDRAFT_00235 | membrane protein insertase, YidC/Oxa1 family, N-terminal domain                           | 1.409   | 0.0846 |
| DespoDRAFT_00236 | hypothetical protein  | 1.628   | 0.42   |
| DespoDRAFT_00237 | ribonuclease P protein component  | 1.099   | 0.42   |
| DespoDRAFT_00238 | ribosomal protein L34, bacterial type   | 1.77    | 0.166  |
| DespoDRAFT_00239 | ribonuclease, Rne/Rng family  | -1.204  | 0.501  |
| DespoDRAFT_00240 | radical SAM-linked protein/radical SAM family uncharacterized protein                     | 1.074   | 0.786  |
| DespoDRAFT_00241 | asparaginyl-tRNA synthetase   | -1.999  | 0.0477 |
| DespoDRAFT_00242 | ribosome small subunit-dependent GTPase A   | -2.198  | 0.0646 |

|                  |  |        |         |
|------------------|--|--------|---------|
| DespoDRAFT_00244 | uncharacterized Blt101-like protein  | -1.981 | 0.344   |
| DespoDRAFT_00245 | FKBP-type peptidyl-prolyl cis-trans isomerase                                  | 2.348  | 0.0541  |
| DespoDRAFT_00246 | response regulator containing a CheY-like receiver domain and an HD-GYP domain | -1.039 | 0.85    |
| DespoDRAFT_00247 | methylase involved in ubiquinone/menaquinone biosynthesis                      | -1.288 | 0.444   |
| DespoDRAFT_00248 | radical SAM domain iron-sulfur cluster-binding oxidoreductase, putative        | 1.068  | 0.827   |
| DespoDRAFT_00249 | tRNA nucleotidyltransferase/poly(A) polymerase                                 | 1.138  | 0.521   |
| DespoDRAFT_00250 | phosphoserine phosphatase SerB   | 1.205  | 0.099   |
| DespoDRAFT_00251 | hypothetical protein   | -1.642 | 0.251   |
| DespoDRAFT_00252 | cold shock protein   | 1.693  | 0.172   |
| DespoDRAFT_00253 | queuosine biosynthesis protein QueC  | 1.603  | 0.309   |
| DespoDRAFT_00254 | organic radical activating enzyme  | 1.682  | 0.0536  |
| DespoDRAFT_00255 | queuosine biosynthesis protein QueD  | 1.12   | 0.818   |
| DespoDRAFT_00256 | homocysteine/selenocysteine methylase (S-methylmethionine-dependent)           | -1.771 | 0.197   |
| DespoDRAFT_00258 | hypothetical protein   | -1.616 | 0.0652  |
| DespoDRAFT_00259 | hypoxanthine phosphoribosyltransferase   | -1.831 | 0.0493  |
| DespoDRAFT_00260 | DnaJ-class molecular chaperone with C-terminal Zn finger domain                | -1.916 | 0.00851 |
| DespoDRAFT_00261 | glucose-inhibited division protein A   | 1.368  | 0.14    |
| DespoDRAFT_00262 | flavoprotein   | 2.148  | 0.387   |
| DespoDRAFT_00263 | ATPase component of ABC transporters with duplicated ATPase domain             | 3.236  | 0.235   |
| DespoDRAFT_00267 | hypothetical protein   | 1.848  | NaN     |
| DespoDRAFT_00269 | diguanylate cyclase (GGDEF) domain-containing protein                          | -2.511 | 0.00271 |
| DespoDRAFT_00270 | aspartate/tyrosine/aromatic aminotransferase                                   | 1.294  | 0.034   |
| DespoDRAFT_00271 | putative Fe-S oxidoreductase   | -1.108 | 0.104   |
| DespoDRAFT_00272 | glutamine synthetase adenylyltransferase                                       | -1.814 | 0.0348  |
| DespoDRAFT_00273 | DisA bacterial checkpoint controller nucleotide-binding protein                | -1.749 | 0.219   |
| DespoDRAFT_00274 | NAD-dependent aldehyde dehydrogenase   | -2.091 | 0.0459  |
| DespoDRAFT_00275 | hypothetical protein   | -2.405 | 0.38    |
| DespoDRAFT_00277 | carbamoyl-phosphate synthase, small subunit                                    | 1.447  | 0.356   |
| DespoDRAFT_00278 | carbamoyl-phosphate synthase, large subunit                                    | 1.108  | 0.149   |
| DespoDRAFT_00279 | amidophosphoribosyltransferase   | 1.949  | 0.159   |
| DespoDRAFT_00280 | putative Fe-S oxidoreductase   | 1.787  | 0.0963  |
| DespoDRAFT_00281 | serine protease inhibitor  | 1.047  | 0.782   |

|                  |  |         |         |
|------------------|--|---------|---------|
| DespoDRAFT_00282 | transposase  | 1.524   | 0.399   |
| DespoDRAFT_00283 | molecular chaperone (small heat shock protein)                             | -4.155  | 0.0612  |
| DespoDRAFT_00284 | molecular chaperone (small heat shock protein)                             | -5.676  | 0.0355  |
| DespoDRAFT_00285 | hypothetical protein   | #VALUE! | NaN     |
| DespoDRAFT_00286 | Pyruvate carboxylase   | 1.318   | 0.0605  |
| DespoDRAFT_00287 | putative N6-adenine-specific DNA methylase                                 | -1.004  | 0.981   |
| DespoDRAFT_00289 | Rhodopirellula transposase   | -2.109  | 0.261   |
| DespoDRAFT_00290 | putative domain HDIG-containing protein                                    | 1.593   | 0.774   |
| DespoDRAFT_00291 | Isocitrate dehydrogenase   | 1.824   | 0.083   |
| DespoDRAFT_00292 | lactate dehydrogenase-like oxidoreductase / Malate dehydrogenase           | -1.262  | 0.164   |
| DespoDRAFT_00294 | transcriptional regulator  | -3.513  | 0.2     |
| DespoDRAFT_00295 | acyl-CoA synthetase (NDP forming)  | -2.668  | 0.0682  |
| DespoDRAFT_00296 | 3-methyl-2-oxobutanoate hydroxymethyltransferase                           | -1.833  | 0.107   |
| DespoDRAFT_00297 | coenzyme F420-dependent NADP oxidoreductase                                | -2.251  | 0.018   |
| DespoDRAFT_00298 | putative Zn-dependent peptidase, insulinase                                | -1.686  | 0.00575 |
| DespoDRAFT_00299 | hypothetical protein   | -2.079  | 0.228   |
| DespoDRAFT_00300 | dimethyladenosine transferase  | -1.751  | 0.0568  |
| DespoDRAFT_00301 | HD-GYP domain-containing protein   | -1.393  | 0.426   |
| DespoDRAFT_00302 | nicotinamidase-like amidase  | -1.154  | 0.74    |
| DespoDRAFT_00303 | nicotinate phosphoribosyltransferase                                       | -1.396  | 0.488   |
| DespoDRAFT_00304 | radical SAM protein, TIGR01212 family                                      | -1.469  | 0.375   |
| DespoDRAFT_00305 | RRM domain-containing RNA-binding protein                                  | 2.997   | 0.33    |
| DespoDRAFT_00306 | putative methyltransferase   | 3.223   | NaN     |
| DespoDRAFT_00307 | hypothetical protein   | 7.816   | 0.0387  |
| DespoDRAFT_00308 | DNA/RNA helicase, superfamily II   | 2.934   | NaN     |
| DespoDRAFT_00309 | cold shock protein   | 5.552   | 0.0834  |
| DespoDRAFT_00310 | Putative exonuclease, RdgC   | 5.54    | 0.0909  |
| DespoDRAFT_00311 | hypothetical protein   | 3.21    | 0.0861  |
| DespoDRAFT_00312 | ribose-phosphate pyrophosphokinase   | 1.789   | 0.199   |
| DespoDRAFT_00314 | peptidyl-prolyl cis-trans isomerase (rotamase) - cyclophilin family        | 2.173   | 0.036   |
| DespoDRAFT_00315 | hypothetical protein   | 3.034   | 0.186   |
| DespoDRAFT_00316 | Na <sup>+</sup> -transporting NADH:ubiquinone oxidoreductase, subunit NqrA | -2.803  | 0.0586  |
| DespoDRAFT_00317 | NADH:ubiquinone oxidoreductase, Na(+)-translocating, B subunit             | -3.02   | 0.16    |
| DespoDRAFT_00318 | Na <sup>+</sup> -transporting NADH:ubiquinone oxidoreductase, subunit NqrC | -2.895  | 0.14    |

|                  |  |         |        |
|------------------|--|---------|--------|
| DespoDRAFT_00319 | NADH:ubiquinone oxidoreductase, Na(+)-translocating, D subunit                       | -4.84   | 0.333  |
| DespoDRAFT_00320 | NADH:ubiquinone oxidoreductase, Na(+)-translocating, E subunit                       | -4.164  | 0.333  |
| DespoDRAFT_00321 | NADH:ubiquinone oxidoreductase, Na(+)-translocating, F subunit                       | -2.005  | 0.0905 |
| DespoDRAFT_00322 | dihydroorotate dehydrogenase family protein  | -1.332  | 0.192  |
| DespoDRAFT_00323 | 2-polyprenylphenol hydroxylase-like oxidoreductase                                   | -1.545  | 0.281  |
| DespoDRAFT_00324 | orotate phosphoribosyltransferase  | -1.495  | 0.103  |
| DespoDRAFT_00325 | periplasmic component of amino acid ABC-type transporter/signal transduction system  | 1.127   | 0.815  |
| DespoDRAFT_00326 | pantothenate kinase, type III  | 1.087   | 0.616  |
| DespoDRAFT_00327 | YbbR-like protein  | 1.597   | 0.606  |
| DespoDRAFT_00328 | dihydropteroate synthase   | 1.214   | 0.13   |
| DespoDRAFT_00329 | ATP-dependent metalloprotease FtsH   | -1.304  | 0.298  |
| DespoDRAFT_00330 | tRNA(Ile)-lysidine synthetase  | 1.301   | 0.33   |
| DespoDRAFT_00331 | O-6-methylguanine DNA methyltransferase  | #VALUE! | NaN    |
| DespoDRAFT_00332 | putative dehydrogenase   | 3.528   | 0.125  |
| DespoDRAFT_00333 | isopropylmalate/homocitrate/citramalate synthase                                     | 3.534   | 0.0616 |
| DespoDRAFT_00334 | hypothetical protein   | -1.508  | 0.246  |
| DespoDRAFT_00335 | molybdenum-pterin binding domain protein   | 1.237   | 0.162  |
| DespoDRAFT_00336 | putative permease  | -1.749  | 0.0466 |
| DespoDRAFT_00337 | Kef-type K <sup>+</sup> transport system, predicted NAD-binding component            | -1.917  | 0.0661 |
| DespoDRAFT_00338 | signal transduction histidine kinase   | -1.087  | 0.892  |
| DespoDRAFT_00339 | response regulator with CheY-like receiver, AAA-type ATPase, and DNA-binding domains | -1.155  | 0.661  |
| DespoDRAFT_00340 | hypothetical protein   | 2.801   | NaN    |
| DespoDRAFT_00341 | potassium uptake protein, TrkH family  | -1.345  | 0.84   |
| DespoDRAFT_00342 | K <sup>+</sup> transport system, NAD-binding component                               | -1.04   | 0.959  |
| DespoDRAFT_00343 | ABC-type multidrug transport system, permease component                              | 1.303   | 0.233  |
| DespoDRAFT_00344 | ABC-type multidrug transport system, permease component                              | 1.247   | 0.513  |
| DespoDRAFT_00345 | ABC-type multidrug transport system, ATPase component                                | 1.045   | 0.633  |
| DespoDRAFT_00346 | multidrug resistance efflux pump   | 1.294   | 0.182  |
| DespoDRAFT_00348 | hypothetical protein   | 1.493   | 0.345  |
| DespoDRAFT_00349 | hypothetical protein   | -1.098  | 0.629  |
| DespoDRAFT_00350 | hypothetical protein   | -1.047  | 0.896  |



|                  |   |        |        |
|------------------|---|--------|--------|
| DespoDRAFT_00354 | hypothetical protein  | -2.552 | 0.0931 |
| DespoDRAFT_00356 | hypothetical protein  | -4.061 | 0.0309 |
| DespoDRAFT_00357 | hypothetical protein  | -2.268 | 0.0838 |
| DespoDRAFT_00358 | restriction endonuclease S subunit  | -2.069 | 0.149  |
| DespoDRAFT_00359 | AAA+ family ATPase  | -2.425 | 0.108  |
| DespoDRAFT_00360 | subtilisin-like serine protease   | -2.537 | 0.0759 |
| DespoDRAFT_00361 | hypothetical protein  | -2.86  | 0.106  |
| DespoDRAFT_00362 | Fic/DOC family protein  | -3.404 | 0.112  |
| DespoDRAFT_00363 | type I site-specific deoxyribonuclease, HsdR family                       | -2.385 | 0.0353 |
| DespoDRAFT_00364 | regulatory P domain of subtilisin-like proprotein convertases             | -3.424 | 0.0568 |
| DespoDRAFT_00365 | hypothetical protein  | 1.033  | 0.835  |
| DespoDRAFT_00366 | putative domain HDIG-containing protein                                   | -1.391 | 0.331  |
| DespoDRAFT_00367 | prepilin-type N-terminal cleavage/methylation domain-containing protein   | -1.782 | 0.185  |
| DespoDRAFT_00368 | Fe-S oxidoreductase   | -2.677 | 0.068  |
| DespoDRAFT_00369 | leucyl aminopeptidase   | -1.667 | 0.128  |
| DespoDRAFT_00370 | A/G-specific adenine glycosylase  | -1.296 | 0.721  |
| DespoDRAFT_00371 | putative transcriptional regulator with HTH domain                        | -1.178 | 0.665  |
| DespoDRAFT_00374 | exonuclease SbcD  | -2.551 | 0.42   |
| DespoDRAFT_00375 | ATPase involved in DNA repair   | -3.437 | 0.518  |
| DespoDRAFT_00376 | methyl-accepting chemotaxis protein                                       | 1.424  | 0.425  |
| DespoDRAFT_00377 | hypothetical protein  | 1.984  | 0.507  |
| DespoDRAFT_00378 | acetyl-CoA hydrolase  | 1.342  | 0.466  |
| DespoDRAFT_00379 | hypothetical protein  | 1.222  | NaN    |
| DespoDRAFT_00380 | hypothetical protein  | 5.061  | NaN    |
| DespoDRAFT_00381 | molybdopterin-guanine dinucleotide biosynthesis protein MobB              | 1.416  | NaN    |
| DespoDRAFT_00382 | hypothetical protein  | 1.491  | 0.72   |
| DespoDRAFT_00383 | pantoate--beta-alanine ligase   | 1.774  | 0.155  |
| DespoDRAFT_00385 | prevent-host-death family protein   | -2.857 | 0.336  |
| DespoDRAFT_00386 | toxin-antitoxin system, toxin component, Txe/YoeB family                  | -2.426 | 0.161  |
| DespoDRAFT_00387 | Kef-type K <sup>+</sup> transport system. predicted NAD-binding component | -1.248 | 0.745  |
| DespoDRAFT_00388 | hypothetical protein  | -1.385 | 0.445  |
| DespoDRAFT_00389 | imidazole glycerol phosphate synthase, glutamine amidotransferase subunit | 1.234  | 0.177  |
| DespoDRAFT_00390 | putative domain HDIG-containing protein                                   | -1.621 | 0.095  |
| DespoDRAFT_00391 | chemotaxis protein  | -1.865 | 0.177  |
| DespoDRAFT_00392 | single stranded DNA-binding protein                                       | -1.178 | 0.146  |
| DespoDRAFT_00393 | DNA gyrase, B subunit   | -1.005 | 0.877  |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_00394 | DNA polymerase III, beta subunit   | 1.199  | 0.231  |
| DespoDRAFT_00395 | hypothetical protein   | -1.57  | 0.0717 |
| DespoDRAFT_00396 | anaerobic ribonucleoside-triphosphate reductase activating protein               | -1.206 | 0.42   |
| DespoDRAFT_00397 | anaerobic ribonucleoside-triphosphate reductase                                  | 1.035  | 0.559  |
| DespoDRAFT_00398 | hypothetical protein   | -1.599 | 0.429  |
| DespoDRAFT_00399 | NTP pyrophosphohydrolase   | -1.752 | 0.324  |
| DespoDRAFT_00400 | molecular chaperone of HSP90 family  | 1.905  | 0.0539 |
| DespoDRAFT_00401 | ribosomal protein S12 methylthiotransferase RimO                                 | 2.192  | 0.145  |
| DespoDRAFT_00402 | geranylgeranyl pyrophosphate synthase  | 2.291  | 0.0725 |
| DespoDRAFT_00403 | hypothetical protein   | 1.918  | 0.0678 |
| DespoDRAFT_00405 | SH3 domain-containing protein  | 1.124  | 0.636  |
| DespoDRAFT_00406 | diguanylate cyclase (GGDEF) domain-containing protein                            | -1.334 | 0.758  |
| DespoDRAFT_00407 | hypothetical protein   | -1.006 | 0.997  |
| DespoDRAFT_00408 | hypothetical protein   | -1.079 | 0.844  |
| DespoDRAFT_00409 | sugar phosphate permease   | -1.124 | 0.877  |
| DespoDRAFT_00410 | 5"/3"-nucleotidase SurE  | -1.056 | 0.724  |
| DespoDRAFT_00411 | transcriptional regulator  | -1.808 | 0.195  |
| DespoDRAFT_00412 | Xaa-Pro aminopeptidase   | -2.401 | 0.193  |
| DespoDRAFT_00413 | indolepyruvate ferredoxin oxidoreductase, alpha/beta subunit                     | 2.005  | 0.112  |
| DespoDRAFT_00414 | 2-oxoacid:ferredoxin oxidoreductase, gamma subunit                               | 3.384  | 0.0842 |
| DespoDRAFT_00415 | coenzyme F390 synthetase   | 1.128  | 0.159  |
| DespoDRAFT_00416 | TRAP-type C4-dicarboxylate transport system, periplasmic component               | 4.295  | 0.0162 |
| DespoDRAFT_00417 | TRAP-type C4-dicarboxylate transport system, small permease component            | 1.937  | 0.112  |
| DespoDRAFT_00418 | TRAP transporter, DctM subunit   | 2.776  | 0.0711 |
| DespoDRAFT_00419 | hypothetical protein   | 1.534  | 0.0859 |
| DespoDRAFT_00420 | ornithine/acetylornithine aminotransferase                                       | 1.674  | 0.183  |
| DespoDRAFT_00421 | hypothetical protein   | -1.537 | 0.164  |
| DespoDRAFT_00423 | integrase family protein   | 1.497  | NaN    |
| DespoDRAFT_00427 | polyphosphate:AMP phosphotransferase   | -1.825 | 0.0451 |
| DespoDRAFT_00428 | HNH endonuclease   | 1.147  | 0.503  |
| DespoDRAFT_00429 | hypothetical protein   | -1.037 | 0.963  |
| DespoDRAFT_00430 | CheY-like receiver domain-containing protein                                     | -2.475 | 0.0378 |
| DespoDRAFT_00431 | glutamate dehydrogenase/leucine dehydrogenase                                    | 1.159  | 0.351  |
| DespoDRAFT_00432 | response regulator containing a CheY-like receiver domain and an HTH DNA-binding | -2.061 | 0.102  |

|                  | domain   |         |        |
|------------------|--|---------|--------|
| DespoDRAFT_00433 | NAD-specific glutamate dehydrogenase   | 1.039   | 0.91   |
| DespoDRAFT_00434 | ABC-type nitrate/sulfonate/bicarbonate transport system, periplasmic component | -3.442  | 0.12   |
| DespoDRAFT_00435 | ABC-type nitrate/sulfonate/bicarbonate transport system, permease component    | -1.704  | 0.627  |
| DespoDRAFT_00436 | ABC-type multidrug transport system, ATPase component                          | -3.054  | 0.494  |
| DespoDRAFT_00437 | putative Fe-S oxidoreductase   | 1.925   | 0.345  |
| DespoDRAFT_00438 | hypothetical protein   | 1.571   | 0.216  |
| DespoDRAFT_00439 | C-terminal processing peptidase  | 1.069   | 0.0417 |
| DespoDRAFT_00440 | membrane-bound metallopeptidase  | 1.14    | 0.124  |
| DespoDRAFT_00441 | cell division protein  | 1.659   | 0.355  |
| DespoDRAFT_00442 | putative ATPase involved in cell division                                      | -1.085  | 0.785  |
| DespoDRAFT_00443 | hydrolase, TatD family   | 2.263   | 0.257  |
| DespoDRAFT_00444 | twin arginine-targeting protein translocase, TatA/E family                     | 1.86    | 0.173  |
| DespoDRAFT_00445 | (protein-PII) uridylyltransferase  | 1.431   | 0.246  |
| DespoDRAFT_00446 | nitrogen regulatory protein PII  | 2.126   | 0.16   |
| DespoDRAFT_00447 | glutamine synthetase, type I   | -1.149  | 0.228  |
| DespoDRAFT_00448 | membrane-bound lytic murein transglycosylase B                                 | 1.438   | 0.597  |
| DespoDRAFT_00449 | hypothetical protein   | -1.415  | 0.812  |
| DespoDRAFT_00451 | extracellular solute-binding protein, family 3                                 | -1.477  | 0.349  |
| DespoDRAFT_00456 | integrase family protein   | -1.691  | 0.553  |
| DespoDRAFT_00457 | hypothetical protein   | #VALUE! | NaN    |
| DespoDRAFT_00459 | PAS domain S-box/diguanylate cyclase (GGDEF) domain-containing protein         | 1.495   | 0.282  |
| DespoDRAFT_00460 | butyrate kinase  | -2.259  | 0.079  |
| DespoDRAFT_00461 | acyl-CoA synthetase/AMP-acid ligase  | -1.749  | 0.0465 |
| DespoDRAFT_00462 | ABC-type multidrug transport system, ATPase and permease component             | -1.493  | 0.335  |
| DespoDRAFT_00463 | ABC-type multidrug transport system, ATPase and permease component             | -1.02   | 0.889  |
| DespoDRAFT_00464 | deoxycytidine triphosphate deaminase   | -1.208  | 0.724  |
| DespoDRAFT_00465 | hypothetical protein   | -1.451  | 0.695  |
| DespoDRAFT_00466 | quinolinate synthetase complex, A subunit                                      | 1.213   | 0.0353 |
| DespoDRAFT_00467 | outer membrane lipoprotein-sorting protein                                     | 1.493   | 0.166  |
| DespoDRAFT_00468 | acyl-CoA synthetase (AMP-forming)/AMP-acid ligase II                           | 1.446   | 0.0223 |
| DespoDRAFT_00469 | chaperone protein DnaK   | 1.115   | 0.497  |
| DespoDRAFT_00470 | molecular chaperone GrpE (heat shock protein)                                  | -2.537  | 0.116  |

|                  |  |        |         |
|------------------|--|--------|---------|
| DespoDRAFT_00472 | anti-anti-sigma regulatory factor (antagonist of anti-sigma factor)                  | -1.629 | 0.324   |
| DespoDRAFT_00473 | hypothetical protein   | -2.092 | 0.112   |
| DespoDRAFT_00474 | hypothetical protein   | -5.042 | 0.209   |
| DespoDRAFT_00475 | NADH:flavin oxidoreductase   | -1.146 | 0.346   |
| DespoDRAFT_00476 | cation diffusion facilitator family transporter                                      | -1.295 | 0.411   |
| DespoDRAFT_00477 | phosphatidylserine synthase  | -1.189 | 0.28    |
| DespoDRAFT_00478 | putative radical SAM protein YgiQ  | -1.027 | 0.925   |
| DespoDRAFT_00479 | arabinose efflux permease family protein   | 1.481  | 0.615   |
| DespoDRAFT_00480 | flagellar motor protein  | -1.66  | 0.726   |
| DespoDRAFT_00481 | flagellar motor component  | -2.568 | 0.302   |
| DespoDRAFT_00482 | acetyl-CoA hydrolase   | -3.153 | 0.0349  |
| DespoDRAFT_00483 | transcription elongation factor  | -1.799 | 0.134   |
| DespoDRAFT_00484 | hypothetical protein   | -3.229 | 0.00283 |
| DespoDRAFT_00485 | response regulator with CheY-like receiver, AAA-type ATPase, and DNA-binding domains | -1.079 | 0.897   |
| DespoDRAFT_00486 | signal transduction histidine kinase   | -1.676 | 0.652   |
| DespoDRAFT_00488 | ABC-type antimicrobial peptide transport system, ATPase component                    | -1.772 | 0.118   |
| DespoDRAFT_00489 | ABC-type transport system, involved in lipoprotein release, permease component       | -1.591 | 0.279   |
| DespoDRAFT_00490 | hypothetical protein   | -1.907 | 0.164   |
| DespoDRAFT_00491 | hypothetical protein   | -1.268 | 0.685   |
| DespoDRAFT_00492 | hypothetical protein   | -1.174 | 0.676   |
| DespoDRAFT_00494 | TIGR04076 family protein   | -1.408 | 0.532   |
| DespoDRAFT_00495 | transcriptional regulator  | -1.319 | 0.616   |
| DespoDRAFT_00496 | RND family efflux transporter, MFP subunit   | -1.772 | 0.257   |
| DespoDRAFT_00497 | ABC-type transport system, involved in lipoprotein release, permease component       | -2.109 | 0.057   |
| DespoDRAFT_00498 | ABC-type antimicrobial peptide transport system, ATPase component                    | -1.223 | 0.756   |
| DespoDRAFT_00499 | efflux transporter, outer membrane factor lipoprotein, NodT family                   | -1.606 | 0.444   |
| DespoDRAFT_00500 | CBS-domain-containing membrane protein   | 3.691  | 0.294   |
| DespoDRAFT_00501 | CBS-domain-containing membrane protein   | 2.01   | 0.443   |
| DespoDRAFT_00502 | hypothetical protein   | -3.393 | 0.0637  |
| DespoDRAFT_00503 | dissimilatory sulfite reductase (desulfovirdin), alpha/beta subunit                  | -1.732 | 0.106   |
| DespoDRAFT_00504 | hypothetical protein   | -1.638 | 0.0635  |
| DespoDRAFT_00505 | nitrate/TMAO reductase, membrane-bound tetraheme cytochrome c subunit                | -4.026 | 0.0609  |
| DespoDRAFT_00506 | PAS domain S-box   | -3.562 | 0.0605  |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_00507 | hydroxylamine reductase  | -3.231 | 0.0416 |
| DespoDRAFT_00508 | beta-lactamase domain protein  | -1.799 | 0.295  |
| DespoDRAFT_00509 | iron-sulfur cluster biosynthesis protein, NifU-like protein                          | 1.525  | 0.424  |
| DespoDRAFT_00510 | universal stress protein UspA-like protein   | -1.225 | 0.691  |
| DespoDRAFT_00511 | pyruvate/2-oxoglutarate dehydrogenase complex, dehydrogenase component alpha subunit | -1.774 | 0.231  |
| DespoDRAFT_00512 | pyruvate/2-oxoglutarate dehydrogenase complex, dehydrogenase component beta subunit  | -1.755 | 0.0956 |
| DespoDRAFT_00513 | CBS-domain-containing membrane protein   | -1.17  | 0.0786 |
| DespoDRAFT_00514 | phosphoenolpyruvate synthase   | -1.184 | 0.432  |
| DespoDRAFT_00515 | Pyruvate ferredoxin oxidoreductase   | -1.277 | 0.143  |
| DespoDRAFT_00516 | hypothetical protein   | -1.702 | 0.0932 |
| DespoDRAFT_00517 | putative sugar kinase  | 1.614  | 0.0853 |
| DespoDRAFT_00518 | phosphoribosylanthranilate isomerase   | 1.77   | 0.154  |
| DespoDRAFT_00519 | threonine dehydrogenase-like Zn-dependent dehydrogenase                              | 2.303  | 0.0857 |
| DespoDRAFT_00520 | DhnA-type fructose-1, 6-bisphosphate aldolase-like enzyme                            | 2.496  | 0.0742 |
| DespoDRAFT_00521 | uncharacterized protein involved in formation of curli polymers                      | 1.386  | 0.0465 |
| DespoDRAFT_00522 | transcriptional regulator  | 1.621  | 0.181  |
| DespoDRAFT_00523 | RND family efflux transporter, MFP subunit   | 1.318  | 0.431  |
| DespoDRAFT_00524 | hydrophobe/amphiphile efflux-1 (HAE1) family transporter                             | 1.456  | 0.14   |
| DespoDRAFT_00525 | efflux transporter, outer membrane factor lipoprotein, NodT family                   | 1.402  | 0.619  |
| DespoDRAFT_00527 | catalase   | -2.708 | 0.045  |
| DespoDRAFT_00528 | alpha/beta superfamily hydrolase   | -2.872 | 0.0736 |
| DespoDRAFT_00530 | cytosine deaminase-like metal-dependent hydrolase                                    | -2.94  | 0.038  |
| DespoDRAFT_00531 | xanthine dehydrogenase, iron-sulfur cluster and FAD-binding subunit A                | -2.85  | 0.108  |
| DespoDRAFT_00532 | xanthine dehydrogenase, molybdopterin-binding subunit B                              | -3.868 | 0.0464 |
| DespoDRAFT_00533 | glutamate dehydrogenase/leucine dehydrogenase  | -2.687 | 0.286  |
| DespoDRAFT_00534 | radical SAM domain iron-sulfur cluster-binding oxidoreductase                        | 1.521  | 0.0951 |
| DespoDRAFT_00535 | glutamate dehydrogenase/leucine dehydrogenase  | -1.536 | 0.134  |
| DespoDRAFT_00536 | ORF6N domain-containing protein  | -2.415 | 0.127  |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_00537 | SagB-type dehydrogenase domain protein   | -3.072 | 0.182  |
| DespoDRAFT_00538 | flagellar protein FlaG   | -2.584 | 0.151  |
| DespoDRAFT_00539 | hypothetical protein   | -1.26  | 0.221  |
| DespoDRAFT_00540 | carbon storage regulator CsrA  | -1.384 | 0.602  |
| DespoDRAFT_00541 | FlgN protein   | -1.413 | 0.505  |
| DespoDRAFT_00542 | Rod binding protein  | 1.342  | 0.685  |
| DespoDRAFT_00543 | flagellar basal-body P-ring protein  | -1.248 | 0.332  |
| DespoDRAFT_00544 | flagellar basal body L-ring protein  | -1.261 | 0.344  |
| DespoDRAFT_00545 | flagella basal body P-ring formation protein FlgA                                  | -1.877 | 0.0162 |
| DespoDRAFT_00546 | flagellar basal-body rod protein FlgG  | -1.618 | 0.0966 |
| DespoDRAFT_00547 | flagellar hook-basal body protein  | -1.596 | 0.139  |
| DespoDRAFT_00548 | uncharacterized protein, cytoplasmic domain of flagellar protein FhlB like protein | -1.101 | 0.956  |
| DespoDRAFT_00549 | Flagellar hook-length control protein FliK   | -1.827 | 0.594  |
| DespoDRAFT_00550 | hypothetical protein   | -1.797 | 0.723  |
| DespoDRAFT_00551 | hypothetical protein   | -4.209 | 0.0834 |
| DespoDRAFT_00552 | hypothetical protein   | -2.806 | 0.0201 |
| DespoDRAFT_00553 | RNA polymerase sigma factor, FliA/WhiG family                                      | -1.475 | 0.339  |
| DespoDRAFT_00554 | ATPase involved in chromosome partitioning   | -2.531 | 0.122  |
| DespoDRAFT_00555 | flagellar GTP-binding protein  | -1.636 | 0.0576 |
| DespoDRAFT_00556 | flagellar biosynthesis protein FlhA  | -1.624 | 0.0662 |
| DespoDRAFT_00557 | flagellar biosynthetic protein FlhB  | -1.823 | 0.457  |
| DespoDRAFT_00558 | flagellar biosynthetic protein FliR  | -1.133 | 0.894  |
| DespoDRAFT_00559 | response regulator containing a CheY-like receiver domain and a GGDEF domain       | -1.247 | 0.547  |
| DespoDRAFT_00560 | Response regulator receiver domain protein, histidine kinase                       | -2.195 | 0.125  |
| DespoDRAFT_00561 | PAS domain S-box   | -1.292 | 0.541  |
| DespoDRAFT_00562 | PAS domain S-box   | -1.225 | 0.499  |
| DespoDRAFT_00563 | flagellar biosynthetic protein FliQ  | -1.086 | 0.88   |
| DespoDRAFT_00564 | flagellar biosynthetic protein FliP  | -1.512 | 0.428  |
| DespoDRAFT_00565 | flagellar biosynthetic protein FliO  | 1.181  | 0.844  |
| DespoDRAFT_00566 | flagellar motor switch protein FliN  | 1.357  | 0.741  |
| DespoDRAFT_00567 | flagellar motor switch protein FliM  | -1.599 | 0.104  |
| DespoDRAFT_00568 | flagellar basal body-associated protein  | -1.598 | 0.083  |
| DespoDRAFT_00569 | flagellar hook-length control protein  | -2.976 | 0.0973 |
| DespoDRAFT_00570 | pyridoxal-phosphate dependent TrpB-like enzyme                                     | 4.516  | 0.0254 |
| DespoDRAFT_00571 | PAS domain S-box   | -1.008 | 0.986  |
| DespoDRAFT_00572 | NAD(P)H-nitrite reductase  | 1.127  | 0.898  |
| DespoDRAFT_00573 | transcriptional regulator  | -2.39  | 0.128  |
| DespoDRAFT_00574 | ketol-acid reductoisomerase  | 2.603  | 0.127  |

|                  |   |         |         |
|------------------|---|---------|---------|
| DespoDRAFT_00575 | serine/threonine protein kinase   | 1.433   | 0.299   |
| DespoDRAFT_00576 | putative phosphoesterase  | -1.112  | 0.923   |
| DespoDRAFT_00577 | cytochrome c peroxidase   | -35.472 | 0.00271 |
| DespoDRAFT_00579 | hypothetical protein  | 1.194   | 0.493   |
| DespoDRAFT_00581 | cold shock protein  | 8.288   | 0.125   |
| DespoDRAFT_00583 | hypothetical protein  | 1.656   | 0.396   |
| DespoDRAFT_00584 | Phytochelatin synthase  | 1.128   | 0.801   |
| DespoDRAFT_00585 | hypothetical protein  | -1.012  | 0.963   |
| DespoDRAFT_00586 | adenylate cyclase   | -1.153  | 0.836   |
| DespoDRAFT_00587 | lipoate synthase  | -1.093  | 0.748   |
| DespoDRAFT_00588 | lipoate-protein ligase B  | -2.217  | 0.131   |
| DespoDRAFT_00589 | putative permease   | -1.103  | 0.512   |
| DespoDRAFT_00590 | hypothetical protein  | 2.093   | 0.0873  |
| DespoDRAFT_00591 | hydro-lyase, Fe-S type, tartrate/fumarate subfamily, hydro-lyase family enzyme, Fe-S type tartrate/fumarate subfamily | 1.601   | 0.0741  |
| DespoDRAFT_00592 | dihydrofolate reductase   | 1.39    | 0.126   |
| DespoDRAFT_00593 | hypothetical protein  | 1.337   | 0.0199  |
| DespoDRAFT_00594 | putative membrane protein   | 1.28    | 0.486   |
| DespoDRAFT_00595 | DNA modification methylase  | 1.49    | 0.0904  |
| DespoDRAFT_00596 | hypothetical protein  | -1.892  | 0.107   |
| DespoDRAFT_00598 | peroxiredoxin   | -1.607  | 0.133   |
| DespoDRAFT_00599 | hypothetical protein  | -1.471  | 0.217   |
| DespoDRAFT_00600 | putative exonuclease of the beta-lactamase fold involved in RNA processing  | -1.508  | 0.147   |
| DespoDRAFT_00601 | hypothetical protein  | -2.082  | 0.14    |
| DespoDRAFT_00603 | ATPase FliI/YscN family   | -2.055  | 0.107   |
| DespoDRAFT_00604 | flagellar biosynthesis/type III secretory pathway protein   | -1.673  | 0.157   |
| DespoDRAFT_00605 | flagellar motor switch protein FliG   | -1.759  | 0.0853  |
| DespoDRAFT_00606 | flagellar basal-body M-ring protein/flagellar hook-basal body protein FliF  | -2.346  | 0.0243  |
| DespoDRAFT_00607 | flagellar hook-basal body complex protein FliE  | -2.762  | 0.119   |
| DespoDRAFT_00608 | flagellar basal-body rod protein FlgC   | -2.927  | 0.034   |
| DespoDRAFT_00609 | flagellar basal-body rod protein FlgB   | -3.635  | 0.0536  |
| DespoDRAFT_00610 | response regulator with CheY-like receiver, AAA-type ATPase, and DNA-binding domains                                  | -1.738  | 0.195   |
| DespoDRAFT_00611 | hypothetical protein  | -2.103  | 0.0957  |
| DespoDRAFT_00612 | response regulator with CheY-like receiver, AAA-type ATPase, and DNA-binding domains                                  | -3.105  | 0.0291  |
| DespoDRAFT_00613 | response regulator with CheY-like receiver, AAA-type ATPase, and DNA-binding domains                                  | -2.852  | 0.0522  |

|                  | domains  |        |         |
|------------------|--|--------|---------|
| DespoDRAFT_00614 | putative inhibitor of MCP methylation, CheC  | -2.746 | 0.0334  |
| DespoDRAFT_00615 | PilZ domain-containing protein   | -4.881 | 0.086   |
| DespoDRAFT_00616 | putative domain HDIG-containing protein  | -3.186 | 0.127   |
| DespoDRAFT_00617 | transcriptional regulator  | -1.21  | 0.61    |
| DespoDRAFT_00618 | diaminopimelate decarboxylase  | 1.001  | 0.987   |
| DespoDRAFT_00619 | acetyl-CoA hydrolase   | -2.092 | 0.197   |
| DespoDRAFT_00620 | tRNA-dihydrouridine synthase   | -1.496 | 0.686   |
| DespoDRAFT_00622 | glycosyl transferase   | 2.364  | 0.0412  |
| DespoDRAFT_00623 | excinuclease ABC, A subunit  | -1.325 | 0.0464  |
| DespoDRAFT_00624 | di-/tricarboxylate transporter   | -1.811 | 0.085   |
| DespoDRAFT_00626 | hypothetical protein   | -2.456 | 0.0896  |
| DespoDRAFT_00627 | hypothetical protein   | -1.638 | 0.0582  |
| DespoDRAFT_00628 | small-conductance mechanosensitive channel   | -1.034 | 0.96    |
| DespoDRAFT_00629 | aspartate/tyrosine/aromatic aminotransferase   | 1.882  | 0.0995  |
| DespoDRAFT_00630 | 3-isopropylmalate dehydrogenase  | 5.944  | 0.00598 |
| DespoDRAFT_00633 | Fumarate hydratase   | -1.884 | 0.2     |
| DespoDRAFT_00634 | hypothetical protein   | -2.255 | 0.0493  |
| DespoDRAFT_00635 | sugar phosphate isomerase/epimerase  | 1.118  | 0.877   |
| DespoDRAFT_00636 | cobalamin biosynthesis protein CobD  | -1.572 | 0.825   |
| DespoDRAFT_00637 | PLP-dependent enzyme, histidinol-phosphate/aromatic aminotransferase or cobyrinic acid decarboxylase | -1.423 | 0.622   |
| DespoDRAFT_00638 | cobalamin-5-phosphate synthase   | -1.207 | 0.811   |
| DespoDRAFT_00639 | adenosyl cobinamide kinase/adenosyl cobinamide phosphate guanylyltransferase                         | -1.236 | 0.672   |
| DespoDRAFT_00640 | hypothetical protein   | 1.76   | NaN     |
| DespoDRAFT_00641 | ParB-like nuclease   | 5.84   | NaN     |
| DespoDRAFT_00642 | hypothetical protein   | -1.396 | 0.649   |
| DespoDRAFT_00644 | putative transcriptional regulator containing CBS domains  | 1.17   | 0.518   |
| DespoDRAFT_00645 | sodium ion-translocating decarboxylase, beta subunit   | -1.169 | 0.442   |
| DespoDRAFT_00646 | hypothetical protein   | -1.455 | 0.396   |
| DespoDRAFT_00647 | acetyl-CoA carboxylase, carboxyltransferase component (subunits alpha and beta)                      | -1.499 | 0.0799  |
| DespoDRAFT_00648 | acetyl/propionyl-CoA carboxylase, alpha subunit  | -1.779 | 0.301   |
| DespoDRAFT_00649 | acyl-CoA dehydrogenase   | -1.448 | 0.143   |
| DespoDRAFT_00650 | ABC-type cobalamin/Fe <sup>3+</sup> -siderophore   | -2.368 | 0.614   |



|                  |  |         |        |
|------------------|--|---------|--------|
|                  | transport system, ATPase component   |         |        |
| DespoDRAFT_00652 | ABC-type Fe <sup>3+</sup> -hydroxamate transport system, periplasmic component     | -1.044  | 0.934  |
| DespoDRAFT_00653 | cytosine deaminase-like metal-dependent hydrolase                                  | 2.685   | 0.33   |
| DespoDRAFT_00654 | hypothetical protein   | -1.912  | 0.201  |
| DespoDRAFT_00655 | hypothetical protein   | -4.763  | 0.0463 |
| DespoDRAFT_00656 | transcriptional regulator containing GAF, AAA-type ATPase, and DNA binding domains | -1.916  | 0.0847 |
| DespoDRAFT_00658 | arabinose efflux permease family protein   | 1.054   | 0.969  |
| DespoDRAFT_00659 | DNA repair protein RadA  | 2.339   | 0.131  |
| DespoDRAFT_00660 | 23S rRNA methylase   | 1.703   | 0.0644 |
| DespoDRAFT_00661 | DNA-binding regulatory protein, YebC/PmpR family                                   | 2.773   | 0.0568 |
| DespoDRAFT_00662 | hypothetical protein   | -1.558  | 0.142  |
| DespoDRAFT_00663 | hypothetical protein   | -2.363  | 0.0681 |
| DespoDRAFT_00664 | hypothetical protein   | -1.045  | 0.982  |
| DespoDRAFT_00665 | transposase family protein   | -1.821  | 0.167  |
| DespoDRAFT_00666 | hypothetical protein   | -1.285  | 0.0958 |
| DespoDRAFT_00667 | NADH:flavin oxidoreductase, flavin dependent.                                      | -1.57   | 0.125  |
| DespoDRAFT_00668 | hypothetical protein   | -1.17   | 0.345  |
| DespoDRAFT_00669 | GTP-binding protein TypA/BipA  | -1.135  | 0.177  |
| DespoDRAFT_00670 | outer membrane lipoprotein   | -1.119  | 0.484  |
| DespoDRAFT_00671 | hypothetical protein   | #VALUE! | NaN    |
| DespoDRAFT_00672 | Protein of unknown function (DUF2589)  | 2.017   | NaN    |
| DespoDRAFT_00673 | hypothetical protein   | 1.276   | 0.104  |
| DespoDRAFT_00674 | uncharacterized protein involved in tellurite resistance                           | -1.055  | 0.533  |
| DespoDRAFT_00675 | hypothetical protein   | -1.141  | 0.277  |
| DespoDRAFT_00676 | hypothetical protein   | -1.33   | 0.095  |
| DespoDRAFT_00677 | putative membrane protein  | -1.382  | 0.263  |
| DespoDRAFT_00678 | putative spermidine synthase with an N-terminal membrane domain                    | -1.203  | 0.804  |
| DespoDRAFT_00679 | primosomal protein N"  | 1.491   | 0.411  |
| DespoDRAFT_00680 | putative ATPase (AAA+ superfamily)   | -1.006  | 0.997  |
| DespoDRAFT_00683 | hypothetical protein   | -1.558  | 0.48   |
| DespoDRAFT_00684 | type I restriction enzyme R protein  | 1.447   | 0.758  |
| DespoDRAFT_00688 | penicillin-binding protein, 1A family  | 1.751   | 0.0557 |
| DespoDRAFT_00690 | phosphoribosyl-AMP cyclohydrolase  | 1.692   | 0.148  |
| DespoDRAFT_00691 | ATP phosphoribosyltransferase  | 1.442   | 0.193  |
| DespoDRAFT_00692 | Aspartate transaminase   | 1.194   | 0.224  |

|                  |   |         |        |
|------------------|---|---------|--------|
| DespoDRAFT_00693 | ribosome biogenesis GTP-binding protein YsxC/EngB                               | 1.072   | 0.921  |
| DespoDRAFT_00694 | GTP-binding protein Era   | 1.297   | 0.323  |
| DespoDRAFT_00695 | restriction endonuclease  | 1.477   | 0.155  |
| DespoDRAFT_00696 | hypothetical protein  | 1.335   | 0.203  |
| DespoDRAFT_00697 | 7-cyano-7-deazaguanine reductase  | 1.395   | 0.767  |
| DespoDRAFT_00698 | putative TIM-barrel protein, nifR3 family                                       | 1.635   | 0.193  |
| DespoDRAFT_00699 | DNA repair photolyase   | 6.477   | 0.227  |
| DespoDRAFT_00700 | hypothetical protein  | 6.561   | 0.122  |
| DespoDRAFT_00701 | PAS domain S-box  | -1.365  | 0.309  |
| DespoDRAFT_00704 | small-conductance mechanosensitive channel                                      | -1.351  | 0.438  |
| DespoDRAFT_00705 | magnesium Mg(2+) and cobalt Co(2+) transport protein CorA                       | -2.084  | 0.219  |
| DespoDRAFT_00706 | Aconitate dehydrogenase   | -2.208  | 0.0586 |
| DespoDRAFT_00707 | K+ transport system, NAD-binding component                                      | -2.197  | 0.155  |
| DespoDRAFT_00708 | nitroreductase  | -1.989  | 0.0231 |
| DespoDRAFT_00709 | acyl-CoA hydrolase  | -1.717  | 0.219  |
| DespoDRAFT_00710 | PEP-CTERM putative exosortase interaction domain-containing protein             | 2.1     | 0.14   |
| DespoDRAFT_00711 | hypothetical protein  | 2.53    | NaN    |
| DespoDRAFT_00712 | Protein of unknown function (DUF2958)   | #VALUE! | NaN    |
| DespoDRAFT_00713 | hypothetical protein  | 3.352   | NaN    |
| DespoDRAFT_00714 | hypothetical protein  | -2.054  | NaN    |
| DespoDRAFT_00715 | antirestriction protein   | -1.415  | 0.886  |
| DespoDRAFT_00716 | hypothetical protein  | 2.878   | NaN    |
| DespoDRAFT_00717 | hypothetical protein  | 1.362   | NaN    |
| DespoDRAFT_00718 | hypothetical protein  | -3.126  | NaN    |
| DespoDRAFT_00719 | hypothetical protein  | #VALUE! | NaN    |
| DespoDRAFT_00720 | hypothetical protein  | 1.247   | 0.914  |
| DespoDRAFT_00721 | hypothetical protein  | -1.562  | 0.586  |
| DespoDRAFT_00722 | bacterial nucleoid DNA-binding protein  | 1.308   | 0.723  |
| DespoDRAFT_00726 | ammonium transporter  | -1.59   | 0.463  |
| DespoDRAFT_00727 | hypothetical protein  | -1.549  | 0.357  |
| DespoDRAFT_00728 | SOS regulatory protein LexA   | -1.825  | 0.146  |
| DespoDRAFT_00729 | hypothetical protein  | -2.209  | 0.0635 |
| DespoDRAFT_00730 | class III cytochrome C family protein   | -1.556  | 0.0325 |
| DespoDRAFT_00731 | ABC-type molybdenum transport system, ATPase component/photorepair protein PhrA | -1.641  | 0.126  |
| DespoDRAFT_00732 | hypothetical protein  | 2.177   | 0.144  |
| DespoDRAFT_00734 | hypothetical protein  | #VALUE! | NaN    |
| DespoDRAFT_00735 | acetyl-CoA acetyltransferase  | -2.184  | 0.0229 |
| DespoDRAFT_00736 | 3-hydroxyacyl-CoA dehydrogenase   | -1.533  | 0.0476 |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_00737 | hypothetical protein   | 1.569  | 0.0829 |
| DespoDRAFT_00738 | hypothetical protein   | 1.99   | 0.175  |
| DespoDRAFT_00739 | PAS domain S-box   | 1.791  | 0.457  |
| DespoDRAFT_00740 | Protein of unknown function (DUF2868)  | 1.004  | 0.957  |
| DespoDRAFT_00741 | protein of unknown function (DUF3482)  | 1.103  | 0.609  |
| DespoDRAFT_00743 | QmoC   | 1.699  | 0.0468 |
| DespoDRAFT_00744 | QmoB / polyferredoxin, heterodixulfide reductase subunit A                         | 1.558  | 0.0952 |
| DespoDRAFT_00745 | QmoA / FAD dependent oxidoreductase  | 1.408  | 0.193  |
| DespoDRAFT_00746 | AprA: adenylylsulfate reductase, alpha subunit                                     | 1.474  | 0.146  |
| DespoDRAFT_00747 | AprB: adenylylsulfate reductase, beta subunit                                      | 1.909  | 0.0447 |
| DespoDRAFT_00748 | putative Fe-S oxidoreductase   | 2.55   | 0.0743 |
| DespoDRAFT_00749 | dehydrogenase of unknown specificity   | 1.325  | 0.591  |
| DespoDRAFT_00750 | transcriptional regulator  | -1.056 | 0.777  |
| DespoDRAFT_00751 | Phosphotransacetylase  | 1.146  | 0.459  |
| DespoDRAFT_00752 | Uncharacterized protein family (UPF0153)   | 2.811  | 0.0634 |
| DespoDRAFT_00753 | deoxyguanosinetriphosphate triphosphohydrolase, putative                           | 1.964  | 0.377  |
| DespoDRAFT_00754 | cytosine/adenosine deaminase   | 1.913  | 0.149  |
| DespoDRAFT_00755 | translation initiation factor IF-3   | 1.472  | 0.538  |
| DespoDRAFT_00756 | ribosomal protein L35  | 3.304  | 0.0161 |
| DespoDRAFT_00757 | ribosomal protein L20  | 2.163  | 0.0241 |
| DespoDRAFT_00758 | phenylalanyl-tRNA synthetase, alpha subunit  | 1.301  | 0.046  |
| DespoDRAFT_00759 | phenylalanyl-tRNA synthetase, beta subunit   | 1.774  | 0.0723 |
| DespoDRAFT_00761 | hypothetical protein   | 1.184  | 0.271  |
| DespoDRAFT_00762 | transcription termination factor NusA  | 1.171  | 0.156  |
| DespoDRAFT_00763 | translation initiation factor IF-2   | 1.153  | 0.327  |
| DespoDRAFT_00764 | ribosome-binding factor A  | 1.042  | 0.752  |
| DespoDRAFT_00765 | tRNA pseudouridine 55 synthase   | 1.226  | 0.482  |
| DespoDRAFT_00766 | ribosomal protein S15  | 2.181  | 0.307  |
| DespoDRAFT_00767 | polyribonucleotide nucleotidyltransferase  | 1.749  | 0.0681 |
| DespoDRAFT_00768 | metal-dependent hydrolase, beta-lactamase superfamily I                            | 1.239  | 0.568  |
| DespoDRAFT_00769 | hypothetical protein   | -2.12  | 0.257  |
| DespoDRAFT_00770 | hypothetical protein   | -1.679 | 0.537  |
| DespoDRAFT_00771 | sigma-54 interacting regulator   | -1.341 | 0.466  |
| DespoDRAFT_00772 | helicase, type I site-specific restriction-modification system restriction subunit | -1.577 | 0.242  |
| DespoDRAFT_00773 | hypothetical protein   | -1.476 | 0.112  |
| DespoDRAFT_00774 | type I restriction-modification system methyltransferase subunit                   | -1.238 | 0.313  |
| DespoDRAFT_00775 | restriction endonuclease S subunit   | -1.466 | 0.352  |

|                  |   |        |        |
|------------------|---|--------|--------|
| DespoDRAFT_00776 | Protein of unknown function (DUF3696)   | -1     | 0.999  |
| DespoDRAFT_00777 | hypothetical protein  | 1.053  | 0.896  |
| DespoDRAFT_00779 | efflux transporter, outer membrane factor lipoprotein, NodT family                | 1.06   | 0.685  |
| DespoDRAFT_00780 | RND family efflux transporter, MFP subunit  | 1.281  | 0.102  |
| DespoDRAFT_00781 | cation/multidrug efflux pump  | 1.815  | 0.283  |
| DespoDRAFT_00783 | xanthine and CO dehydrogenases maturation factor, XdhC/CoxF family                | -1.051 | 0.494  |
| DespoDRAFT_00784 | putative MobA-like protein  | 1.213  | 0.16   |
| DespoDRAFT_00785 | fructose-2, 6-bisphosphatase  | -1.913 | 0.345  |
| DespoDRAFT_00786 | NAD-dependent aldehyde dehydrogenase  | -1.65  | 0.0242 |
| DespoDRAFT_00787 | aerobic-type carbon monoxide dehydrogenase, large subunit CoxL/CutL-like protein  | 1.008  | 0.964  |
| DespoDRAFT_00789 | hypothetical protein  | -1.571 | NaN    |
| DespoDRAFT_00791 | methylase involved in ubiquinone/menaquinone biosynthesis                         | 1.459  | 0.455  |
| DespoDRAFT_00792 | molecular chaperone (small heat shock protein)                                    | 1.452  | 0.516  |
| DespoDRAFT_00793 | molecular chaperone (small heat shock protein)                                    | 1.193  | 0.822  |
| DespoDRAFT_00793 | formylmethanofuran dehydrogenase subunit E  | 1.747  | 0.48   |
| DespoDRAFT_00795 | TRAP transporter, DctM subunit  | 3.327  | 0.161  |
| DespoDRAFT_00796 | TRAP-type C4-dicarboxylate transport system, small permease component             | 3.377  | 0.117  |
| DespoDRAFT_00797 | TRAP-type C4-dicarboxylate transport system, periplasmic component                | 1.491  | 0.0194 |
| DespoDRAFT_00798 | diguanylate cyclase (GGDEF) domain/uncharacterized domain HDIG-containing protein | -1.544 | 0.503  |
| DespoDRAFT_00799 | hydrogenase maturation protease   | -4.665 | 0.0881 |
| DespoDRAFT_00800 | Ni, Fe-hydrogenase I large subunit  | -1.897 | 0.0791 |
| DespoDRAFT_00801 | hydrogenase (NiFe) small subunit HydA   | -1.556 | 0.143  |
| DespoDRAFT_00802 | hypothetical protein  | -2.497 | 0.124  |
| DespoDRAFT_00803 | acyl-CoA thioester hydrolase, YbgC/YbaW family                                    | 1.226  | 0.721  |
| DespoDRAFT_00804 | nitroreductase  | 1.157  | 0.697  |
| DespoDRAFT_00805 | soluble P-type ATPase   | 1.422  | 0.498  |
| DespoDRAFT_00806 | Acetate kinase  | 1.142  | 0.2    |
| DespoDRAFT_00807 | crcB protein ; Cis-regulatory element   | -1.506 | 0.696  |
| DespoDRAFT_00808 | hypothetical protein  | -1.65  | 0.411  |
| DespoDRAFT_00809 | response regulator with CheY-like receiver, AAA-type ATPase, and DNA-binding      | -1.396 | 0.122  |

|                  |   |         |        |
|------------------|---|---------|--------|
|                  | domains   |         |        |
| DespoDRAFT_00810 | acetate--CoA ligase   | 1.011   | 0.717  |
| DespoDRAFT_00811 | apsK ATP sulphurylase/adenylylsulfate kinase  | -1.373  | 0.17   |
| DespoDRAFT_00812 | putative Zn-dependent hydrolase of beta-lactamase fold                              | 1.044   | 0.832  |
| DespoDRAFT_00813 | Fe-S-cluster-containing hydrogenase subunit   | 2.088   | 0.0362 |
| DespoDRAFT_00814 | hypothetical protein  | -1.126  | 0.194  |
| DespoDRAFT_00815 | putative domain HDIG-containing protein   | -1.067  | 0.435  |
| DespoDRAFT_00816 | family 3 adenylate cyclase  | -1.096  | 0.818  |
| DespoDRAFT_00817 | response regulator receiver domain protein  | -1.976  | 0.344  |
| DespoDRAFT_00818 | adenylate cyclase   | -2.318  | 0.392  |
| DespoDRAFT_00819 | HDOD domain-containing protein  | -1.847  | 0.181  |
| DespoDRAFT_00820 | hypothetical protein  | 1.235   | 0.804  |
| DespoDRAFT_00821 | putative transcriptional regulator  | 7.106   | 0.0789 |
| DespoDRAFT_00822 | homoaconitate hydratase family protein/3-isopropylmalate dehydratase, large subunit | 4.791   | 0.037  |
| DespoDRAFT_00823 | 3-isopropylmalate dehydratase, small subunit  | 5.844   | 0.0439 |
| DespoDRAFT_00824 | hypothetical protein  | 1.637   | 0.419  |
| DespoDRAFT_00825 | hypothetical protein  | 2.22    | 0.248  |
| DespoDRAFT_00826 | putative amidophosphoribosyltransferase   | 1.331   | 0.641  |
| DespoDRAFT_00827 | hypothetical protein  | -1.037  | 0.93   |
| DespoDRAFT_00828 | hypothetical protein  | -1.57   | 0.0947 |
| DespoDRAFT_00830 | NAD(+) kinase   | #VALUE! | 1      |
| DespoDRAFT_00831 | DNA polymerase I  | 1.455   | 0.338  |
| DespoDRAFT_00832 | hypothetical protein  | 1.982   | 0.135  |
| DespoDRAFT_00833 | phosphoribosylglycinamide formyltransferase, formyltetrahydrofolate-dependent       | 2.172   | 0.158  |
| DespoDRAFT_00834 | putative signal transduction protein containing EAL and modified HD-GYP domains     | 1.778   | 0.282  |
| DespoDRAFT_00835 | pheromone shutdown-related protein TraB   | 1.333   | 0.241  |
| DespoDRAFT_00836 | hypothetical protein  | 1.06    | 0.89   |
| DespoDRAFT_00837 | hypothetical protein  | -1.006  | 0.979  |
| DespoDRAFT_00838 | DNA repair protein RecN   | 1.041   | 0.482  |
| DespoDRAFT_00839 | putative regulatory protein, FmdB family  | -1.031  | 0.929  |
| DespoDRAFT_00840 | glycerophosphoryl diester phosphodiesterase   | -1.579  | 0.209  |
| DespoDRAFT_00844 | acyl dehydratase  | -1.199  | 0.537  |
| DespoDRAFT_00845 | PAS domain S-box  | -2.262  | 0.0572 |
| DespoDRAFT_00846 | acyl-CoA dehydrogenase  | 2.301   | 0.101  |

|                  |  |        |         |
|------------------|--|--------|---------|
| DespoDRAFT_00847 | acetyl-CoA acetyltransferase   | 2.749  | 0.0467  |
| DespoDRAFT_00848 | 3-hydroxyacyl-CoA dehydrogenase  | 2.339  | 0.0687  |
| DespoDRAFT_00849 | metal-dependent hydrolase, beta-lactamase superfamily II   | -1.235 | 0.846   |
| DespoDRAFT_00850 | putative permease  | 1.298  | 0.449   |
| DespoDRAFT_00851 | enoyl-CoA hydratase/carnithine racemase  | -1.516 | 0.28    |
| DespoDRAFT_00852 | arabinose efflux permease family protein   | -1.858 | 0.0912  |
| DespoDRAFT_00853 | DNA/RNA helicase, superfamily I  | -1.085 | 0.876   |
| DespoDRAFT_00854 | phosphomannomutase   | 1.033  | 0.731   |
| DespoDRAFT_00855 | putative bacitracin resistance protein   | 1.87   | 0.472   |
| DespoDRAFT_00856 | outer membrane protein/peptidoglycan-associated (lipo)protein  | 1.251  | 0.14    |
| DespoDRAFT_00857 | DnaK suppressor protein  | 1.157  | 0.661   |
| DespoDRAFT_00858 | LL-diaminopimelate aminotransferase  | 1.029  | 0.857   |
| DespoDRAFT_00859 | hypothetical protein   | 1.953  | 0.085   |
| DespoDRAFT_00860 | Glutamine amidotransferases class-II   | 4.667  | 0.0303  |
| DespoDRAFT_00861 | glutamate synthase family protein  | 2.647  | 0.0438  |
| DespoDRAFT_00862 | NADPH-dependent glutamate synthase beta chain-like oxidoreductase  | 2.667  | 0.00525 |
| DespoDRAFT_00863 | bacteriocin propeptide, TIGR03798 family   | -2.213 | 0.182   |
| DespoDRAFT_00864 | molybdenum ABC transporter, periplasmic molybdate-binding protein  | -1.335 | 0.107   |
| DespoDRAFT_00865 | CysU ABC-type sulfate transport system, permease component (molybdate ABC transporter, permease protein) | -1.061 | 0.884   |
| DespoDRAFT_00866 | molybdenum ABC transporter, ATP-binding protein  | -1.285 | 0.42    |
| DespoDRAFT_00867 | CoA-substrate-specific enzyme activase, putative   | 2.254  | 0.214   |
| DespoDRAFT_00868 | hypothetical protein   | 1.028  | 0.983   |
| DespoDRAFT_00869 | putative RND superfamily exporter  | -4.662 | 0.276   |
| DespoDRAFT_00870 | hypothetical protein   | -1.795 | 0.41    |
| DespoDRAFT_00871 | putative hydrolase or acyltransferase of alpha/beta superfamily  | -1.057 | 0.612   |
| DespoDRAFT_00872 | Zn-dependent protease with chaperone function  | -1.583 | 0.0613  |
| DespoDRAFT_00874 | transcriptional regulator  | 1.28   | 0.471   |
| DespoDRAFT_00875 | 1, 4-alpha-glucan branching enzyme   | -4.66  | 0.0572  |
| DespoDRAFT_00876 | glycogen/starch/alpha-glucan phosphorylase   | -4.513 | 0.0145  |
| DespoDRAFT_00877 | 1, 4-alpha-glucan branching enzyme   | -2.188 | 0.0512  |
| DespoDRAFT_00878 | glycogen synthase  | -3.248 | 0.112   |
| DespoDRAFT_00879 | glycogen debranching enzyme  | -4.953 | 0.0222  |
| DespoDRAFT_00880 | aspartate-semialdehyde dehydrogenase, gamma-proteobacterial  | 2.103  | 0.0508  |
| DespoDRAFT_00881 | collagenase-like protease  | -1.136 | 0.71    |

|                  |  |        |         |
|------------------|--|--------|---------|
| DespoDRAFT_00882 | phosphomethylpyrimidine kinase   | -1.937 | 0.0645  |
| DespoDRAFT_00885 | methyl-accepting chemotaxis protein  | -2.842 | 0.449   |
| DespoDRAFT_00886 | putative NAD(P)H quinone oxidoreductase, PIG3 family   | -1.235 | 0.0661  |
| DespoDRAFT_00887 | amino acid transporter   | -1.03  | 0.942   |
| DespoDRAFT_00888 | RND family efflux transporter, MFP subunit   | -1.58  | 0.338   |
| DespoDRAFT_00889 | hydrophobe/amphiphile efflux-1 (HAE1) family transporter/efflux transporter, outer membrane factor (OMF) lipoprotein NodT fam> | -1.289 | 0.257   |
| DespoDRAFT_00890 | methyltransferase family protein   | -1.346 | 0.783   |
| DespoDRAFT_00891 | hypothetical protein   | 1.334  | 0.303   |
| DespoDRAFT_00892 | hypothetical protein   | -1.109 | 0.76    |
| DespoDRAFT_00893 | hypothetical protein   | -1.253 | 0.685   |
| DespoDRAFT_00894 | dienelactone hydrolase-like enzyme   | -1.848 | 0.0813  |
| DespoDRAFT_00895 | cobalamin biosynthesis protein CbiK, Co2+ chelatase  | 1.353  | 0.26    |
| DespoDRAFT_00896 | ABC-type Fe3+-siderophore transport system, permease component   | 1.061  | 0.61    |
| DespoDRAFT_00897 | ABC-type cobalamin/Fe3+-siderophore transport system, ATPase component   | 1.334  | 0.653   |
| DespoDRAFT_00898 | ABC-type Fe3+-hydroxamate transport system, periplasmic component  | 1.76   | 0.316   |
| DespoDRAFT_00899 | cobyrinic acid a, c-diamide synthase   | 1.375  | 0.32    |
| DespoDRAFT_00900 | precorrin isomerase  | -1.541 | 0.00435 |
| DespoDRAFT_00901 | precorrin-2 C20-methyltransferase  | -1.087 | 0.69    |
| DespoDRAFT_00902 | hypothetical protein   | 1.276  | 0.845   |
| DespoDRAFT_00903 | cobalamin biosynthesis protein CbiD  | -1.832 | 0.394   |
| DespoDRAFT_00904 | type I site-specific deoxyribonuclease, HsdR family  | -1.042 | 0.917   |
| DespoDRAFT_00905 | restriction endonuclease S subunit   | -1.198 | 0.909   |
| DespoDRAFT_00906 | type I restriction system adenine methylase HsdM   | 1.428  | 0.583   |
| DespoDRAFT_00907 | hypothetical protein   | -2.868 | NaN     |
| DespoDRAFT_00908 | putative periplasmic lipoprotein (DUF2279)   | 1.209  | 0.818   |
| DespoDRAFT_00909 | precorrin-6y C5, 15-methyltransferase (decarboxylating), CbiE subunit, precorrin-6Y C5, 15-methyltransferase (decarboxylating) | -1.068 | 0.836   |
| DespoDRAFT_00910 | hypothetical protein   | -1.218 | 0.793   |
| DespoDRAFT_00911 | growth inhibitor   | -1.619 | 0.105   |
| DespoDRAFT_00912 | precorrin-4 C11-methyltransferase  | -2.148 | 0.136   |
| DespoDRAFT_00913 | cobalamin biosynthesis protein CbiG  | -1.569 | 0.665   |
| DespoDRAFT_00914 | precorrin-3B C17-methyltransferase   | -2.001 | 0.527   |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_00915 | cobyric acid synthase CobQ   | -1.988 | 0.24   |
| DespoDRAFT_00916 | Helix-turn-helix protein   | -2.237 | 0.622  |
| DespoDRAFT_00917 | HipA-like protein  | -4.008 | 0.112  |
| DespoDRAFT_00918 | universal stress protein UspA-like protein   | -4.033 | 0.172  |
| DespoDRAFT_00919 | hypothetical protein   | -2.699 | 0.194  |
| DespoDRAFT_00920 | methyltransferase, cyclopropane fatty acid synthase                                  | -1.955 | 0.0854 |
| DespoDRAFT_00921 | flavin-dependent dehydrogenase   | -1.555 | 0.147  |
| DespoDRAFT_00922 | molybdopterin biosynthesis enzyme  | -1.344 | 0.262  |
| DespoDRAFT_00923 | response regulator with CheY-like receiver, AAA-type ATPase, and DNA-binding domains | -2.205 | 0.159  |
| DespoDRAFT_00924 | PAS domain S-box   | -3.622 | 0.112  |
| DespoDRAFT_00925 | hypothetical protein   | -3.619 | 0.12   |
| DespoDRAFT_00926 | hypothetical protein   | -2.594 | 0.108  |
| DespoDRAFT_00927 | putative permease  | -1.464 | 0.143  |
| DespoDRAFT_00928 | hypothetical protein   | -1.508 | 0.112  |
| DespoDRAFT_00929 | NADPH-dependent glutamate synthase beta chain-like oxidoreductase                    | -3.808 | 0.03   |
| DespoDRAFT_00930 | Fe-S-cluster-containing hydrogenase subunit  | -5.659 | 0.0421 |
| DespoDRAFT_00931 | Thiosulfate reductase, putative  | -5.702 | 0.0162 |
| DespoDRAFT_00932 | putative membrane-bound metal-dependent hydrolase (DUF457)                           | -1.608 | 0.477  |
| DespoDRAFT_00933 | alanine dehydrogenase  | -1.977 | 0.135  |
| DespoDRAFT_00934 | putative SAM-dependent methyltransferase   | 1.296  | 0.449  |
| DespoDRAFT_00935 | hypothetical protein   | -1.044 | 0.928  |
| DespoDRAFT_00936 | putative N6-adenine-specific DNA methylase   | 2.748  | 0.11   |
| DespoDRAFT_00937 | putative regulatory protein, FmdB family   | 3.532  | 0.127  |
| DespoDRAFT_00938 | hypothetical protein   | 5.855  | 0.1    |
| DespoDRAFT_00939 | dinitrogenase iron-molybdenum cofactor biosynthesis protein                          | 6.845  | 0.0473 |
| DespoDRAFT_00940 | P-loop ATPase, MinD superfamily  | 4.29   | 0.02   |
| DespoDRAFT_00941 | P-loop ATPase, MinD superfamily  | 3.522  | 0.0463 |
| DespoDRAFT_00942 | hypothetical protein   | 1.605  | 0.175  |
| DespoDRAFT_00943 | phospho-2-dehydro-3-deoxyheptonate aldolase  | 3.068  | 0.126  |
| DespoDRAFT_00944 | protein of unknown function (DUF697)   | 1.17   | 0.702  |
| DespoDRAFT_00945 | hypothetical protein   | -1.403 | 0.635  |
| DespoDRAFT_00946 | hypothetical protein   | -1.023 | 0.973  |
| DespoDRAFT_00947 | hypothetical protein   | 1.459  | 0.398  |
| DespoDRAFT_00948 | hypothetical protein   | -1.137 | 0.825  |
| DespoDRAFT_00949 | hypothetical protein   | -1.419 | 0.677  |
| DespoDRAFT_00950 | hypothetical protein   | -1.765 | 0.691  |



|                  |   |         |        |
|------------------|---|---------|--------|
| DespoDRAFT_00951 | putative membrane protein   | -3.745  | 0.181  |
| DespoDRAFT_00952 | hypothetical protein  | #VALUE! | NaN    |
| DespoDRAFT_00953 | putative RNA-binding protein containing KH domain, possibly ribosomal protein         | 1.314   | 0.333  |
| DespoDRAFT_00954 | Zn-dependent hydrolase, glyoxylase  | -1.164  | 0.347  |
| DespoDRAFT_00955 | GTP-binding protein YchF  | 1.319   | 0.41   |
| DespoDRAFT_00956 | hypothetical protein  | -1.12   | 0.652  |
| DespoDRAFT_00957 | molybdenum cofactor synthesis domain protein  | 1.085   | 0.722  |
| DespoDRAFT_00958 | pyrimidine operon attenuation protein/uracil phosphoribosyltransferase                | -1.092  | 0.594  |
| DespoDRAFT_00959 | molybdopterin-guanine dinucleotide biosynthesis protein A                             | -1.516  | 0.153  |
| DespoDRAFT_00960 | molybdopterin converting factor, large subunit  | -1.573  | 0.138  |
| DespoDRAFT_00961 | molybdenum cofactor biosynthesis protein MoaC   | -1.622  | 0.201  |
| DespoDRAFT_00962 | hypothetical protein  | -1.293  | 0.166  |
| DespoDRAFT_00963 | membrane-bound lytic murein transglycosylase  | -1.011  | 0.931  |
| DespoDRAFT_00964 | hypothetical protein  | -3.744  | 0.235  |
| DespoDRAFT_00965 | histidine kinase, Response regulator receiver domain protein                          | -11.152 | 0.128  |
| DespoDRAFT_00966 | hypothetical protein  | -17.009 | 0.107  |
| DespoDRAFT_00967 | hypothetical protein  | -1.226  | NaN    |
| DespoDRAFT_00968 | methyl-accepting chemotaxis protein   | -2.031  | 0.0477 |
| DespoDRAFT_00969 | Hpt domain-containing protein   | -2.121  | 0.158  |
| DespoDRAFT_00970 | response regulator containing a CheY-like receiver domain and an HD-GYP domain        | -2.027  | 0.146  |
| DespoDRAFT_00971 | hypothetical protein  | -2.74   | 0.493  |
| DespoDRAFT_00972 | phosphate transport system regulatory protein PhoU                                    | 2.75    | 0.0578 |
| DespoDRAFT_00973 | response regulator with CheY-like receiver domain and winged-helix DNA-binding domain | -1.212  | 0.557  |
| DespoDRAFT_00974 | PAS domain S-box  | 1.257   | 0.442  |
| DespoDRAFT_00976 | Plasmid pRiA4b ORF-3-like protein   | 1.199   | 0.504  |
| DespoDRAFT_00977 | hypothetical protein  | -1.733  | 0.106  |
| DespoDRAFT_00978 | ATPase involved in DNA repair   | 1.476   | 0.401  |
| DespoDRAFT_00979 | TIGR02436 family protein  | 2.683   | 0.48   |
| DespoDRAFT_00980 | exonuclease SbcD  | -1.13   | 0.508  |
| DespoDRAFT_00981 | hypothetical protein  | -1.182  | 0.672  |
| DespoDRAFT_00982 | restriction endonuclease  | 1.46    | 0.247  |
| DespoDRAFT_00983 | hypothetical protein  | #VALUE! | NaN    |
| DespoDRAFT_00984 | hypothetical protein  | 1.217   | 0.47   |

|                  |   |        |        |
|------------------|---|--------|--------|
| DespoDRAFT_00985 | hypothetical protein  | 1.301  | 0.367  |
| DespoDRAFT_00986 | adenine specific DNA methylase Mod  | 1.327  | 0.388  |
| DespoDRAFT_00987 | hypothetical protein  | -1.046 | 0.937  |
| DespoDRAFT_00988 | DNA/RNA helicase, superfamily II, SNF2 family                                     | 1.137  | 0.42   |
| DespoDRAFT_00989 | DNA-binding protein, excisionase family   | 1.518  | 0.35   |
| DespoDRAFT_00990 | putative addiction module killer protein  | -1.375 | 0.431  |
| DespoDRAFT_00991 | putative addiction module antidote protein  | -1.751 | 0.0496 |
| DespoDRAFT_00992 | putative TIM-barrel fold metal-dependent hydrolase                                | 1.128  | 0.335  |
| DespoDRAFT_00993 | siroheme synthase, N-terminal domain  | 1.219  | 0.0936 |
| DespoDRAFT_00994 | ABC-type transport system involved in cytochrome c biogenesis, permease component | -1.184 | 0.332  |
| DespoDRAFT_00995 | glutamyl-tRNA reductase   | 1.428  | 0.108  |
| DespoDRAFT_00996 | penicillin-binding protein 1B   | 1.242  | 0.423  |
| DespoDRAFT_00997 | hypothetical protein  | 2.602  | 0.311  |
| DespoDRAFT_00998 | hypothetical protein  | -1     | 0.999  |
| DespoDRAFT_01000 | ABC-type Fe <sup>3+</sup> transport system, permease component                    | 1.257  | 0.756  |
| DespoDRAFT_01001 | hypothetical protein  | 1.26   | 0.284  |
| DespoDRAFT_01002 | acyl-CoA synthetase (AMP-forming)/AMP-acid ligase II                              | 2.072  | 0.0644 |
| DespoDRAFT_01003 | cupin domain-containing protein   | 3.164  | 0.0728 |
| DespoDRAFT_01004 | signal transduction histidine kinase  | 1.26   | 0.448  |
| DespoDRAFT_01005 | HRDC domain-containing protein  | 1.244  | 0.732  |
| DespoDRAFT_01006 | hypothetical protein  | -1.12  | 0.893  |
| DespoDRAFT_01007 | DNA/RNA helicase, superfamily II SNF2 family                                      | 1.377  | 0.262  |
| DespoDRAFT_01008 | DNA-methyltransferase Dcm   | 1.12   | 0.818  |
| DespoDRAFT_01009 | DNA mismatch endonuclease Vsr   | -1.085 | 0.854  |
| DespoDRAFT_01010 | hypothetical protein  | -1.318 | 0.623  |
| DespoDRAFT_01011 | plasmid maintenance system killer protein   | 1.224  | 0.705  |
| DespoDRAFT_01012 | addiction module antidote protein, HigA family                                    | 1.419  | 0.668  |
| DespoDRAFT_01014 | cold shock protein  | -2.354 | 0.107  |
| DespoDRAFT_01015 | DNA/RNA helicase superfamily II   | 1.956  | 0.0897 |
| DespoDRAFT_01016 | hypothetical protein  | 6.635  | 0.249  |
| DespoDRAFT_01017 | hypothetical protein  | -1.352 | NaN    |
| DespoDRAFT_01018 | 23S RNA-specific pseudouridylate synthase   | 1.502  | 0.556  |
| DespoDRAFT_01020 | Alkaline phosphatase  | 1.632  | 0.394  |
| DespoDRAFT_01021 | putative multitransmembrane protein   | -1.011 | 0.987  |
| DespoDRAFT_01022 | putative Zn-dependent protease  | -1.306 | 0.0838 |
| DespoDRAFT_01023 | general secretion pathway protein F   | 1.109  | 0.741  |
| DespoDRAFT_01024 | hypothetical protein  | 1.384  | 0.147  |

|                  |   |        |        |
|------------------|---|--------|--------|
| DespoDRAFT_01025 | Sulfate ATPase (ABC-type multidrug transport system ATPase component)     | -1.341 | 0.0625 |
| DespoDRAFT_01026 | ABC-type multidrug transport system permease component                    | -1.655 | 0.673  |
| DespoDRAFT_01027 | phosphoesterase MJ0936 family   | -1.793 | 0.337  |
| DespoDRAFT_01028 | Zn-dependent protease with chaperone function                             | 1.196  | 0.672  |
| DespoDRAFT_01029 | bacterial nucleoid DNA-binding protein                                    | 3.879  | 0.0123 |
| DespoDRAFT_01030 | adenylosuccinate lyase  | 1.073  | 0.361  |
| DespoDRAFT_01031 | uncharacterized protein PH0010 family                                     | 1.155  | 0.218  |
| DespoDRAFT_01032 | TrpR-related protein YerC/YecD  | -1.888 | 0.0681 |
| DespoDRAFT_01033 | putative phosphoesterase (MutT family)                                    | 1.003  | 0.987  |
| DespoDRAFT_01034 | hypothetical protein  | 1.447  | 0.493  |
| DespoDRAFT_01036 | nucleoside-diphosphate-sugar epimerase                                    | -1.735 | 0.209  |
| DespoDRAFT_01037 | putative membrane protein   | -1.409 | 0.53   |
| DespoDRAFT_01038 | putative signal transduction protein                                      | -1.242 | 0.503  |
| DespoDRAFT_01039 | protein affecting phage T7 exclusion by the F plasmid                     | -1.858 | 0.104  |
| DespoDRAFT_01040 | leucyl/phenylalanyl-tRNA--protein transferase                             | -1.206 | 0.369  |
| DespoDRAFT_01041 | ATP-dependent Clp protease ATP-binding subunit clpA                       | -1.941 | 0.0651 |
| DespoDRAFT_01042 | hypothetical protein  | -1.089 | 0.776  |
| DespoDRAFT_01043 | preprotein translocase SecA subunit                                       | -1.447 | 0.108  |
| DespoDRAFT_01044 | metalloendopeptidase-like membrane protein                                | -1.289 | 0.233  |
| DespoDRAFT_01045 | N-acetyl-gamma-glutamyl-phosphate reductase common form                   | 1.905  | 0.023  |
| DespoDRAFT_01046 | putative phosphatase C-terminal domain of histone macro H2A1 like protein | -1.86  | 0.112  |
| DespoDRAFT_01047 | TRAP transporter solute receptor TAXI family                              | 1.189  | 0.086  |
| DespoDRAFT_01048 | TRAP transporter 4TM/12TM fusion protein                                  | -1.782 | 0.127  |
| DespoDRAFT_01049 | universal stress protein UspA-like protein                                | -1.545 | 0.0657 |
| DespoDRAFT_01051 | NTP pyrophosphohydrolase  | -1.562 | 0.172  |
| DespoDRAFT_01052 | Zn-dependent protease with chaperone function                             | -1.213 | 0.436  |
| DespoDRAFT_01053 | hypothetical protein  | 2.504  | 0.149  |
| DespoDRAFT_01054 | iron-sulfur cluster biosynthesis protein NifU-like protein                | 2.672  | 0.0828 |
| DespoDRAFT_01055 | putative RNA-binding protein (contains KH domain)                         | -1.885 | 0.365  |
| DespoDRAFT_01056 | ABC-type uncharacterized transport system periplasmic component           | -1.982 | 0.0852 |

|                  |  |        |         |
|------------------|--|--------|---------|
| DespoDRAFT_01057 | hypothetical protein   | -1.106 | 0.847   |
| DespoDRAFT_01058 | arabinose efflux permease family protein   | 1.237  | 0.823   |
| DespoDRAFT_01059 | putative amino acid racemase   | 1.273  | 0.686   |
| DespoDRAFT_01060 | serine phosphatase RsbU regulator of sigma subunit                                 | -1.292 | 0.61    |
| DespoDRAFT_01061 | serine phosphatase RsbU regulator of sigma subunit                                 | -1.115 | 0.909   |
| DespoDRAFT_01062 | Protein of unknown function (DUF3124)  | -1.178 | 0.498   |
| DespoDRAFT_01063 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains | -2.381 | 0.0828  |
| DespoDRAFT_01064 | GSPII_E-like protein   | -1.847 | 0.0881  |
| DespoDRAFT_01065 | ATPase involved in chromosome partitioning   | -2.166 | 0.106   |
| DespoDRAFT_01066 | beta-hydroxyacid dehydrogenase, 3-hydroxyisobutyrate dehydrogenase                 | -1.36  | 0.261   |
| DespoDRAFT_01067 | pterin-4a-carbinolamine dehydratase  | -3.703 | 0.00938 |
| DespoDRAFT_01068 | drug resistance transporter, Bcr/CflA subfamily                                    | -1.984 | 0.143   |
| DespoDRAFT_01069 | putative membrane protein  | -2.132 | 0.0591  |
| DespoDRAFT_01070 | nucleotidyltransferase/DNA polymerase involved in DNA repair                       | -1.961 | 0.205   |
| DespoDRAFT_01071 | ABC-type dipeptide transport system, periplasmic component                         | 2.635  | 0.0698  |
| DespoDRAFT_01072 | oligopeptide/dipeptide ABC transporter, ATP-binding protein                        | 1.922  | 0.38    |
| DespoDRAFT_01073 | cold shock protein   | 1.2    | 0.417   |
| DespoDRAFT_01074 | oligopeptide/dipeptide ABC transporter, ATP-binding protein                        | 2.655  | 0.214   |
| DespoDRAFT_01075 | hypothetical protein   | -2.6   | NaN     |
| DespoDRAFT_01076 | hypothetical protein   | 1.082  | 0.777   |
| DespoDRAFT_01077 | parvulin-like peptidyl-prolyl isomerase  | 1.288  | 0.0326  |
| DespoDRAFT_01078 | Mg <sup>2+</sup> transporter MgtE  | -1.106 | 0.713   |
| DespoDRAFT_01079 | DNA repair protein RecO  | 1.924  | 0.251   |
| DespoDRAFT_01080 | putative kinase, galactokinase/mevalonate kinase                                   | 1.031  | 0.918   |
| DespoDRAFT_01081 | hypothetical protein   | 1.284  | 0.207   |
| DespoDRAFT_01082 | uridine phosphorylase  | 1.129  | 0.603   |
| DespoDRAFT_01083 | DNA ligase, NAD-dependent  | -1.027 | 0.824   |
| DespoDRAFT_01084 | signal recognition particle-docking protein FtsY                                   | 1.67   | 0.122   |
| DespoDRAFT_01085 | diguanylate cyclase (GGDEF) domain-containing protein                              | -1.12  | 0.687   |
| DespoDRAFT_01086 | 6-phosphofructokinase  | -1.211 | 0.464   |

|                  |   |        |        |
|------------------|---|--------|--------|
| DespoDRAFT_01087 | putative heme d1 biosynthesis radical SAM protein NirJ2                             | -1.184 | 0.141  |
| DespoDRAFT_01088 | delta-aminolevulinic acid dehydratase   | 1.109  | 0.468  |
| DespoDRAFT_01089 | putative heme d1 biosynthesis radical SAM protein NirJ1                             | 1.545  | 0.0302 |
| DespoDRAFT_01090 | ATP-dependent protease Clp, ATPase subunit  | -1.773 | 0.0682 |
| DespoDRAFT_01091 | hypothetical protein  | 3.746  | 0.291  |
| DespoDRAFT_01093 | protein translocase, SecE subunit   | 1.459  | 0.0316 |
| DespoDRAFT_01094 | triosephosphate isomerase   | 1.628  | 0.42   |
| DespoDRAFT_01095 | glyceraldehyde-3-phosphate dehydrogenase, type I                                    | 1.391  | 0.188  |
| DespoDRAFT_01096 | phosphotransferase system, mannose/fructose-specific component IIA                  | 1.186  | 0.534  |
| DespoDRAFT_01097 | putative P-loop-containing kinase   | -1.227 | 0.134  |
| DespoDRAFT_01098 | phosphotransferase system mannitol/fructose-specific IIA component (Ntr-type)       | -1.075 | 0.77   |
| DespoDRAFT_01099 | ribosomal subunit interface protein   | 1.184  | 0.325  |
| DespoDRAFT_01100 | RNA polymerase sigma-54 factor  | 1.125  | 0.116  |
| DespoDRAFT_01101 | ABC-type (unclassified) transport system, ATPase component                          | -1.041 | 0.228  |
| DespoDRAFT_01102 | hypothetical protein  | 1.03   | 0.851  |
| DespoDRAFT_01103 | hypothetical protein  | 1.79   | 0.374  |
| DespoDRAFT_01104 | 3-deoxy-D-manno-octulosonate 8-phosphate phosphatase, YrbI family                   | 2.318  | 0.0682 |
| DespoDRAFT_01105 | 3-deoxy-8-phosphooctulonate synthase  | 2.932  | 0.0893 |
| DespoDRAFT_01106 | metalloendopeptidase-like membrane protein  | 1.022  | 0.867  |
| DespoDRAFT_01107 | hypothetical protein  | -1.025 | 0.671  |
| DespoDRAFT_01108 | signal peptidase I  | -1.084 | 0.851  |
| DespoDRAFT_01109 | aspartate carbamoyltransferase  | 1.268  | 0.169  |
| DespoDRAFT_01110 | dihydroorotase, multifunctional complex type  | 1.31   | 0.0424 |
| DespoDRAFT_01111 | hypothetical protein  | -1.343 | 0.394  |
| DespoDRAFT_01112 | hypothetical protein  | -1.137 | 0.751  |
| DespoDRAFT_01113 | response regulator with CheY-like receiver, AAA-type ATPase and DNA-binding domains | -1.123 | 0.505  |
| DespoDRAFT_01114 | prepilin-type N-terminal cleavage/methylation domain-containing protein             | -4.713 | 0.0511 |
| DespoDRAFT_01115 | ABC-type multidrug transport system, ATPase component                               | -2.311 | 0.0347 |
| DespoDRAFT_01116 | hypothetical protein  | -2.695 | 0.0936 |

|                  |   |        |        |
|------------------|---|--------|--------|
| DespoDRAFT_01117 | hypothetical protein  | -1.72  | 0.329  |
| DespoDRAFT_01118 | Protein of unknown function (DUF2893)   | -1.418 | 0.471  |
| DespoDRAFT_01119 | protein of unknown function (DUF1814)   | -1.634 | 0.568  |
| DespoDRAFT_01121 | prevent-host-death family protein   | -1.243 | 0.852  |
| DespoDRAFT_01123 | restriction endonuclease  | 1.3    | 0.498  |
| DespoDRAFT_01124 | hypothetical protein  | 1.151  | 0.783  |
| DespoDRAFT_01125 | hypothetical protein  | 1.778  | 0.578  |
| DespoDRAFT_01126 | hypothetical protein  | -1.087 | 0.832  |
| DespoDRAFT_01127 | hypothetical protein  | -1.96  | 0.042  |
| DespoDRAFT_01128 | hypothetical protein  | -1.143 | 0.847  |
| DespoDRAFT_01129 | hypothetical protein  | -1.246 | 0.513  |
| DespoDRAFT_01130 | hypothetical protein  | -1.724 | 0.188  |
| DespoDRAFT_01131 | hypothetical protein  | -1.843 | 0.0405 |
| DespoDRAFT_01132 | prepilin-type N-terminal cleavage/methylation domain-containing protein         | -2.348 | 0.0824 |
| DespoDRAFT_01133 | prepilin-type N-terminal cleavage/methylation domain-containing protein         | -3.092 | 0.168  |
| DespoDRAFT_01134 | prepilin-type N-terminal cleavage/methylation domain-containing protein         | -3.758 | 0.128  |
| DespoDRAFT_01135 | thiamine biosynthesis protein ThiC  | 1.23   | 0.196  |
| DespoDRAFT_01136 | hypothetical protein  | 1.4    | 0.0644 |
| DespoDRAFT_01137 | phosphopantothenoylecysteine decarboxylase/phosphopantothenate--cysteine ligase | 1.01   | 0.778  |
| DespoDRAFT_01138 | uracil-DNA glycosylase  | 1.651  | 0.0757 |
| DespoDRAFT_01139 | site-specific recombinase XerD  | -1.046 | 0.871  |
| DespoDRAFT_01140 | ATP-dependent protease HslVU, peptidase subunit                                 | 1.282  | 0.298  |
| DespoDRAFT_01141 | ATP-dependent protease HslVU, ATPase subunit                                    | 2.049  | 0.0841 |
| DespoDRAFT_01142 | acetylglutamate kinase  | 1.505  | 0.0477 |
| DespoDRAFT_01143 | acetylornithine/succinylornithine aminotransferase                              | 1.505  | 0.261  |
| DespoDRAFT_01144 | ornithine carbamoyltransferase  | 1.565  | 0.17   |
| DespoDRAFT_01145 | argininosuccinate lyase   | 1.48   | 0.2    |
| DespoDRAFT_01146 | hypothetical protein  | 1.715  | 0.0462 |
| DespoDRAFT_01147 | 2-amino-4-hydroxy-6-hydroxymethyl-dihydropteridine pyrophosphokinase            | 6.107  | 0.0248 |
| DespoDRAFT_01148 | fructose-6-phosphate aldolase, TalC/MipB family                                 | 4.815  | 0.029  |
| DespoDRAFT_01151 | hypothetical protein  | -1.827 | 0.231  |

|                  |   |         |        |
|------------------|---|---------|--------|
| DespoDRAFT_01155 | putative transcriptional regulator                                    | 1.129   | NaN    |
| DespoDRAFT_01156 | DNA polymerase III epsilon subunit-like 3'-5' exonuclease             | -1.146  | 0.963  |
| DespoDRAFT_01157 | hypothetical protein  | 1.119   | NaN    |
| DespoDRAFT_01158 | phage regulatory protein, rha family                                  | -1.564  | 0.856  |
| DespoDRAFT_01159 | CO dehydrogenase maturation factor                                    | -1.284  | NaN    |
| DespoDRAFT_01161 | type IV secretory pathway, VirB2 component (pilin)                    | -1.646  | NaN    |
| DespoDRAFT_01162 | type IV secretory pathway, VirB4 component                            | -1.517  | 0.809  |
| DespoDRAFT_01163 | P-type conjugative transfer protein TrbJ                              | -3.766  | 0.216  |
| DespoDRAFT_01164 | hypothetical protein  | -3.369  | 0.136  |
| DespoDRAFT_01165 | P-type conjugative transfer protein TrbL                              | 1.173   | 0.944  |
| DespoDRAFT_01166 | type IV secretory pathway, TrbF component                             | -1.401  | 0.847  |
| DespoDRAFT_01167 | P-type conjugative transfer protein TrbG                              | -1.096  | 0.972  |
| DespoDRAFT_01168 | Conjugal transfer protein TrbH  | -2.003  | NaN    |
| DespoDRAFT_01169 | type IV secretory pathway, VirB10 component                           | -1.85   | 0.796  |
| DespoDRAFT_01170 | DNA topoisomerase III   | -1.19   | 0.921  |
| DespoDRAFT_01171 | hypothetical protein  | 1.447   | 0.682  |
| DespoDRAFT_01172 | antirestriction protein   | -1.129  | 0.931  |
| DespoDRAFT_01173 | type IV secretory pathway, VirD4 component                            | -1.506  | 0.805  |
| DespoDRAFT_01174 | type IV secretory pathway, protease TraF                              | 1.746   | NaN    |
| DespoDRAFT_01175 | P-type conjugative transfer ATPase TrbB                               | -1.401  | 0.749  |
| DespoDRAFT_01176 | Ribbon-helix-helix protein, copG family                               | #VALUE! | NaN    |
| DespoDRAFT_01177 | relaxase/mobilization nuclease  | 1.056   | 0.972  |
| DespoDRAFT_01178 | hypothetical protein  | -1.635  | NaN    |
| DespoDRAFT_01179 | cytotoxic translational repressor of toxin-antitoxin stability system | -3.567  | 0.0993 |
| DespoDRAFT_01180 | putative transcriptional regulator with C-terminal CBS domains        | -3.341  | 0.0464 |
| DespoDRAFT_01181 | hypothetical protein  | -2.276  | 0.148  |
| DespoDRAFT_01182 | hypothetical protein  | -2.548  | 0.142  |
| DespoDRAFT_01183 | methylase involved in ubiquinone/menaquinone biosynthesis             | -2.45   | 0.134  |
| DespoDRAFT_01184 | DnaJ-class molecular chaperone with C-terminal Zn finger domain       | -1.743  | 0.435  |
| DespoDRAFT_01185 | hypothetical protein  | 1.144   | 0.827  |
| DespoDRAFT_01186 | serine/threonine protein kinase                                       | -1.082  | 0.929  |
| DespoDRAFT_01187 | hypothetical protein  | 1.513   | 0.631  |
| DespoDRAFT_01188 | putative ATPase   | 1.485   | 0.359  |
| DespoDRAFT_01189 | hypothetical protein  | 2.151   | 0.42   |
| DespoDRAFT_01190 | hypothetical protein  | 1.202   | 0.48   |

|                  |  |         |        |
|------------------|--|---------|--------|
| DespoDRAFT_01191 | hypothetical protein   | -1.107  | 0.842  |
| DespoDRAFT_01192 | hypothetical protein   | 1.091   | 0.911  |
| DespoDRAFT_01193 | S23 ribosomal protein  | -3.178  | 0.0202 |
| DespoDRAFT_01194 | hypothetical protein   | -1.802  | 0.109  |
| DespoDRAFT_01195 | putative transcriptional regulator with HTH domain               | -1.59   | 0.0571 |
| DespoDRAFT_01196 | hypothetical protein   | -1.096  | 0.685  |
| DespoDRAFT_01197 | hypothetical protein   | 1.103   | 0.537  |
| DespoDRAFT_01198 | restriction endonuclease S subunit                               | 1.009   | 0.946  |
| DespoDRAFT_01199 | type I restriction-modification system methyltransferase subunit | -1.001  | 0.999  |
| DespoDRAFT_01200 | hypothetical protein   | -2.087  | 0.066  |
| DespoDRAFT_01201 | hypothetical protein   | -1.251  | 0.315  |
| DespoDRAFT_01202 | type I restriction-modification system methyltransferase subunit | 1.528   | 0.171  |
| DespoDRAFT_01203 | hypothetical protein   | #VALUE! | NaN    |
| DespoDRAFT_01204 | hypothetical protein   | -5.136  | NaN    |
| DespoDRAFT_01206 | site-specific recombinase XerD                                   | -2.702  | 0.135  |
| DespoDRAFT_01207 | hypothetical protein   | 3.24    | 0.173  |
| DespoDRAFT_01208 | DNA polymerase III epsilon subunit-like 3'-5' exonuclease        | 3.171   | 0.435  |
| DespoDRAFT_01209 | hypothetical protein   | -1.425  | NaN    |
| DespoDRAFT_01210 | phage regulatory protein, rha family                             | 3.686   | 0.219  |
| DespoDRAFT_01211 | CobQ/CobB/MinD/ParA nucleotide binding domain-containing protein | -1.134  | 0.913  |
| DespoDRAFT_01212 | hypothetical protein   | -1.054  | 0.971  |
| DespoDRAFT_01213 | type IV secretory pathway, VirB2 component (pilin)               | 2.495   | NaN    |
| DespoDRAFT_01215 | Rhodopirellula transposase                                       | -1.452  | 0.832  |
| DespoDRAFT_01216 | P-type conjugative transfer protein TrbJ                         | -1.349  | 0.867  |
| DespoDRAFT_01217 | hypothetical protein   | -5.2    | 0.234  |
| DespoDRAFT_01218 | P-type conjugative transfer protein TrbL                         | 2.139   | NaN    |
| DespoDRAFT_01219 | type IV secretory pathway, TrbF component                        | 2.336   | NaN    |
| DespoDRAFT_01220 | P-type conjugative transfer protein TrbG                         | 8.646   | NaN    |
| DespoDRAFT_01221 | Conjugal transfer protein TrbH                                   | #VALUE! | NaN    |
| DespoDRAFT_01222 | type IV secretory pathway, VirB10 component                      | 1.117   | 0.968  |
| DespoDRAFT_01223 | hypothetical protein   | -1.912  | NaN    |
| DespoDRAFT_01224 | DNA topoisomerase III  | -1.433  | 0.751  |
| DespoDRAFT_01225 | hypothetical protein   | -5.004  | 0.11   |
| DespoDRAFT_01226 | antirestriction protein  | -1.424  | 0.808  |
| DespoDRAFT_01227 | type IV secretory pathway, VirD4 component                       | -1.28   | 0.818  |
| DespoDRAFT_01228 | type IV secretory pathway, protease TraF                         | -1.193  | 0.875  |



|                  |  |         |        |
|------------------|--|---------|--------|
| DespoDRAFT_01229 | P-type conjugative transfer ATPase TrbB                          | -1.343  | 0.903  |
| DespoDRAFT_01230 | TrbM   | -2.5    | 0.574  |
| DespoDRAFT_01231 | Ribbon-helix-helix protein, copG family                          | 3.056   | NaN    |
| DespoDRAFT_01232 | relaxase/mobilization nuclease                                   | -1.322  | 0.696  |
| DespoDRAFT_01233 | hypothetical protein   | 1.216   | 0.718  |
| DespoDRAFT_01234 | nuclease-like protein protein kinase family protein              | 1.012   | 0.98   |
| DespoDRAFT_01238 | hypothetical protein   | -1.244  | 0.707  |
| DespoDRAFT_01239 | abortive infection bacteriophage resistance protein              | -1.078  | 0.934  |
| DespoDRAFT_01240 | putative metal-dependent hydrolase                               | 1.797   | 0.177  |
| DespoDRAFT_01241 | type I site-specific deoxyribonuclease HsdR family               | 1.081   | 0.827  |
| DespoDRAFT_01242 | restriction endonuclease S subunit                               | -1.613  | 0.485  |
| DespoDRAFT_01243 | type I restriction-modification system methyltransferase subunit | 2.242   | 0.14   |
| DespoDRAFT_01244 | secondary thiamine-phosphate synthase enzyme                     | -1.645  | 0.373  |
| DespoDRAFT_01245 | hypothetical protein   | -2.104  | 0.122  |
| DespoDRAFT_01248 | hypothetical protein   | -1.144  | 0.828  |
| DespoDRAFT_01250 | transposase  | #VALUE! | NaN    |
| DespoDRAFT_01252 | hypothetical protein   | -1.402  | 0.583  |
| DespoDRAFT_01253 | site-specific recombinase XerD                                   | -1.323  | 0.747  |
| DespoDRAFT_01254 | regulator of stationary/sporulation gene expression              | -1.58   | 0.387  |
| DespoDRAFT_01255 | putative nucleic-acid-binding protein                            | -1.739  | 0.195  |
| DespoDRAFT_01257 | hypothetical protein   | -1.565  | 0.248  |
| DespoDRAFT_01260 | tyrosyl-tRNA synthetase  | 1.659   | 0.432  |
| DespoDRAFT_01261 | nicotinamidase-like amidase                                      | -1.436  | 0.283  |
| DespoDRAFT_01262 | putative permease  | -1.597  | 0.486  |
| DespoDRAFT_01263 | Protein of unknown function (DUF3124)                            | -1.349  | 0.545  |
| DespoDRAFT_01264 | hypothetical protein   | -1.584  | 0.421  |
| DespoDRAFT_01265 | hypothetical protein   | -1.454  | 0.227  |
| DespoDRAFT_01266 | hypothetical protein   | -1.901  | 0.444  |
| DespoDRAFT_01267 | Protein of unknown function (DUF3102)                            | -1.658  | 0.61   |
| DespoDRAFT_01268 | hypothetical protein   | -1.57   | 0.424  |
| DespoDRAFT_01269 | putative transcription factor, MBF1 like protein                 | 1.811   | NaN    |
| DespoDRAFT_01270 | hypothetical protein   | -2.496  | 0.586  |
| DespoDRAFT_01272 | hypothetical protein   | 1.34    | 0.706  |
| DespoDRAFT_01273 | hypothetical protein   | -1.092  | 0.893  |
| DespoDRAFT_01274 | hypothetical protein   | -1.345  | 0.758  |
| DespoDRAFT_01275 | hypothetical protein   | -2.93   | 0.0594 |
| DespoDRAFT_01276 | hypothetical protein   | -1.634  | 0.464  |
| DespoDRAFT_01277 | hypothetical protein   | 1.641   | 0.334  |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_01278 | site-specific recombinase XerD   | -1.395 | 0.746  |
| DespoDRAFT_01279 | hypothetical protein   | 2.091  | NaN    |
| DespoDRAFT_01280 | hypothetical protein   | 1.007  | NaN    |
| DespoDRAFT_01281 | hypothetical protein   | -1.535 | 0.847  |
| DespoDRAFT_01282 | hypothetical protein   | -1.155 | 0.952  |
| DespoDRAFT_01283 | hypothetical protein   | 1.508  | 0.622  |
| DespoDRAFT_01284 | site-specific recombinase, DNA invertase Pin   | -1.435 | 0.471  |
| DespoDRAFT_01286 | transposase  | -1.012 | 0.963  |
| DespoDRAFT_01287 | glycogen synthase  | -2.281 | 0.189  |
| DespoDRAFT_01288 | acetyl-CoA hydrolase   | -2.386 | 0.0837 |
| DespoDRAFT_01289 | Kef-type K <sup>+</sup> transport system, predicted NAD-binding component            | -1.865 | 0.166  |
| DespoDRAFT_01290 | cyclic nucleotide-binding protein  | -1.95  | 0.402  |
| DespoDRAFT_01291 | transcription elongation factor  | -1.778 | 0.247  |
| DespoDRAFT_01292 | Ribosomal protein S27  | -1.819 | 0.133  |
| DespoDRAFT_01293 | hypothetical protein   | -2.655 | 0.0608 |
| DespoDRAFT_01294 | hypothetical protein   | -4.583 | 0.0637 |
| DespoDRAFT_01295 | response regulator with CheY-like receiver, AAA-type ATPase, and DNA-binding domains | 1.361  | 0.771  |
| DespoDRAFT_01297 | di-/tricarboxylate transporter   | -2.514 | 0.504  |
| DespoDRAFT_01298 | hypothetical protein   | -1.98  | 0.27   |
| DespoDRAFT_01299 | glyceraldehyde-3-phosphate dehydrogenase type I                                      | -1.267 | 0.345  |
| DespoDRAFT_01300 | dehydrogenase of unknown specificity   | -1.415 | 0.14   |
| DespoDRAFT_01301 | glycogen/starch/alpha-glucan phosphorylase   | -1.415 | 0.489  |
| DespoDRAFT_01302 | membrane protein MarC family   | -1.049 | 0.921  |
| DespoDRAFT_01303 | hypothetical protein   | -1.926 | 0.701  |
| DespoDRAFT_01306 | hypothetical protein   | 1.706  | NaN    |
| DespoDRAFT_01307 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains   | -1.355 | 0.728  |
| DespoDRAFT_01309 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains   | -2.644 | 0.619  |
| DespoDRAFT_01310 | signal transduction histidine kinase   | -1.246 | 0.826  |
| DespoDRAFT_01311 | iron-sulfur cluster repair di-iron protein   | -2.623 | 0.0636 |
| DespoDRAFT_01312 | hypothetical protein   | -4.595 | 0.129  |
| DespoDRAFT_01313 | transcriptional regulator  | -2.622 | 0.0489 |
| DespoDRAFT_01314 | RND family efflux transporter MFP subunit  | -2.927 | 0.187  |
| DespoDRAFT_01315 | ABC-type transport system involved in lipoprotein release permease component         | -2.674 | 0.0489 |

|                  |  |         |        |
|------------------|--|---------|--------|
| DespoDRAFT_01316 | ABC-type antimicrobial peptide transport system ATPase component                   | -2.608  | 0.111  |
| DespoDRAFT_01317 | efflux transporter outer membrane factor lipoprotein NodT family                   | -2.044  | 0.316  |
| DespoDRAFT_01318 | polyferredoxin   | 1.573   | 0.719  |
| DespoDRAFT_01320 | hypothetical protein   | -3.653  | 0.0475 |
| DespoDRAFT_01321 | hypothetical protein   | -1.005  | 0.997  |
| DespoDRAFT_01322 | Retron-type reverse transcriptase  | -1.2    | 0.746  |
| DespoDRAFT_01324 | Retron-type reverse transcriptase  | -1.919  | 0.352  |
| DespoDRAFT_01327 | Protein of unknown function (DUF1566)  | -1.166  | 0.769  |
| DespoDRAFT_01328 | copper/silver-translocating P-type ATPase  | -1.466  | 0.128  |
| DespoDRAFT_01329 | hypothetical protein   | -3.195  | 0.0574 |
| DespoDRAFT_01330 | hypothetical protein   | -6.784  | 0.0951 |
| DespoDRAFT_01331 | putative membrane protein  | -9.034  | 0.212  |
| DespoDRAFT_01332 | Positive regulator of sigma E activity   | -9.733  | 0.106  |
| DespoDRAFT_01333 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains | -1.206  | 0.645  |
| DespoDRAFT_01334 | histidine kinase   | -1.357  | 0.538  |
| DespoDRAFT_01336 | hypothetical protein   | -1.132  | 0.934  |
| DespoDRAFT_01337 | hypothetical protein   | -5.431  | 0.0531 |
| DespoDRAFT_01338 | nitrate/TMAO reductase membrane-bound tetraheme cytochrome c subunit               | -3.72   | 0.125  |
| DespoDRAFT_01339 | PAS domain S-box   | -3.166  | 0.084  |
| DespoDRAFT_01340 | hydroxylamine reductase  | -2.691  | 0.126  |
| DespoDRAFT_01341 | putative Nitric oxide reductase  | -3.154  | 0.08   |
| DespoDRAFT_01342 | hydrid cluster protein-associated redox disulfide domain                           | -1.365  | 0.748  |
| DespoDRAFT_01343 | cAMP-binding protein   | 1.103   | 0.931  |
| DespoDRAFT_01346 | hypothetical protein   | -2.015  | NaN    |
| DespoDRAFT_01347 | site-specific recombinase XerD   | -3.553  | 0.199  |
| DespoDRAFT_01349 | hypothetical protein   | 1.045   | NaN    |
| DespoDRAFT_01350 | hypothetical protein   | 1.815   | 0.47   |
| DespoDRAFT_01352 | hypothetical protein   | -3.126  | NaN    |
| DespoDRAFT_01353 | hypothetical protein   | -1.784  | 0.284  |
| DespoDRAFT_01354 | diaminopimelate epimerase  | -2.047  | 0.256  |
| DespoDRAFT_01355 | hypothetical protein   | -11.838 | 0.0298 |
| DespoDRAFT_01356 | hypothetical protein   | -1.796  | 0.219  |
| DespoDRAFT_01357 | DNA/RNA helicase superfamily I   | -1.433  | 0.237  |
| DespoDRAFT_01358 | hypothetical protein   | 1.103   | 0.804  |
| DespoDRAFT_01359 | soluble lytic murein transglycosylase-like protein                                 | -1.453  | 0.125  |
| DespoDRAFT_01360 | UTP-glucose-1-phosphate uridylyltransferase  | -1.794  | 0.0981 |
| DespoDRAFT_01361 | putative Fe-S oxidoreductase   | 1.357   | 0.21   |

|                  |   |        |        |
|------------------|---|--------|--------|
| DespoDRAFT_01362 | dihydrodipicolinate synthase  | 1.385  | 0.187  |
| DespoDRAFT_01363 | putative selenocysteine protein   | 1.875  | 0.108  |
| DespoDRAFT_01364 | dsrA: sulfite reductase, dissimilatory-type alpha subunit               | 2.575  | 0.0326 |
| DespoDRAFT_01365 | dsrB: sulfite reductase, dissimilatory-type beta subunit                | 2.194  | 0.0834 |
| DespoDRAFT_01366 | dsrD: sulfite reductase, dissimilatory-type delta subunit               | 1.172  | 0.212  |
| DespoDRAFT_01367 | cobyrinic acid a c-diamide synthase                                     | 1.259  | 0.183  |
| DespoDRAFT_01368 | putative xylanase/chitin deacetylase                                    | 1.748  | 0.283  |
| DespoDRAFT_01370 | hypothetical protein  | -2.37  | 0.0603 |
| DespoDRAFT_01371 | putative membrane protein involved in D-alanine export                  | 1.335  | 0.62   |
| DespoDRAFT_01372 | hypothetical protein  | -1.255 | 0.575  |
| DespoDRAFT_01373 | hypothetical protein  | -2.596 | NaN    |
| DespoDRAFT_01374 | radical SAM additional 4Fe4S-binding domain protein                     | 1.812  | 0.465  |
| DespoDRAFT_01375 | MMPL family   | 1.276  | 0.605  |
| DespoDRAFT_01376 | glycosyltransferase involved in LPS biosynthesis                        | 1.743  | 0.394  |
| DespoDRAFT_01377 | putative membrane protein   | 1.524  | 0.623  |
| DespoDRAFT_01378 | hypothetical protein  | 1.355  | 0.362  |
| DespoDRAFT_01379 | hypothetical protein  | -1.302 | 0.431  |
| DespoDRAFT_01380 | acyl carrier protein  | -1.289 | 0.503  |
| DespoDRAFT_01381 | soluble lytic murein transglycosylase-like protein                      | -1.861 | 0.138  |
| DespoDRAFT_01382 | hypothetical protein  | 1.038  | 0.924  |
| DespoDRAFT_01383 | hypothetical protein  | -1.169 | 0.498  |
| DespoDRAFT_01384 | 3-hydroxymyristoyl/3-hydroxydecanoyl-(acyl carrier protein) dehydratase | -1.085 | 0.781  |
| DespoDRAFT_01385 | acyl carrier protein  | 1.19   | 0.714  |
| DespoDRAFT_01386 | EDD domain protein DegV family  | 1.518  | 0.346  |
| DespoDRAFT_01387 | putative thioesterase   | 1.391  | 0.658  |
| DespoDRAFT_01388 | hypothetical protein  | 2.826  | 0.104  |
| DespoDRAFT_01389 | 3-oxoacyl-(acyl-carrier-protein) synthase                               | 1.282  | 0.306  |
| DespoDRAFT_01390 | Tfp pilus assembly protein PilF   | -1.046 | 0.199  |
| DespoDRAFT_01391 | hypothetical protein  | -1.901 | 0.0729 |
| DespoDRAFT_01392 | hypothetical protein  | -2.685 | 0.0895 |
| DespoDRAFT_01393 | methylase involved in ubiquinone/menaquinone biosynthesis               | 1.075  | 0.834  |
| DespoDRAFT_01394 | hypothetical protein  | 2.694  | 0.0435 |
| DespoDRAFT_01395 | acetyl-CoA synthetase (AMP-forming)/AMP-acid ligase II                  | 2.521  | 0.082  |
| DespoDRAFT_01396 | 3-oxoacyl-(acyl-carrier-protein) synthase                               | 2.416  | 0.227  |
| DespoDRAFT_01397 | 1-acyl-sn-glycerol-3-phosphate  | 1.414  | 0.622  |

|                  |   |        |          |
|------------------|---|--------|----------|
|                  | acyltransferase   |        |          |
| DespoDRAFT_01398 | 3-oxoacyl-(acyl-carrier-protein) synthase   | 2.401  | 0.29     |
| DespoDRAFT_01399 | 3-oxoacyl-(acyl-carrier-protein) synthase   | 2.383  | 0.0965   |
| DespoDRAFT_01400 | acyl-CoA thioester hydrolase YbgC/YbaW family   | 2.304  | 0.424    |
| DespoDRAFT_01401 | hypothetical protein  | 2.595  | 0.023    |
| DespoDRAFT_01402 | glycosyl transferase  | 2.25   | 0.122    |
| DespoDRAFT_01403 | Lauroyl/myristoyl acyltransferase   | -1.123 | 0.856    |
| DespoDRAFT_01404 | UDP-N-acetylmuramyl pentapeptide phosphotransferase/UDP-N-acetylglucosamine-1-phosphate transferase | 1.393  | 0.476    |
| DespoDRAFT_01405 | NAD dependent epimerase/dehydratase family protein  | 1.765  | 0.471    |
| DespoDRAFT_01406 | UDP-N-acetylglucosamine 1-carboxyvinyltransferase   | 1.401  | 0.0634   |
| DespoDRAFT_01407 | DNA internalization-related competence protein ComEC/Rec2   | -1.658 | 0.449    |
| DespoDRAFT_01408 | hypothetical protein  | -1.039 | 0.935    |
| DespoDRAFT_01409 | CoA-substrate-specific enzyme activase putative   | -1.61  | 0.0463   |
| DespoDRAFT_01410 | putative integral membrane protein  | 1.248  | 0.63     |
| DespoDRAFT_01411 | CysA: sulfate/thiosulfate import ATP-binding protein CysA   | 1.418  | 0.184    |
| DespoDRAFT_01412 | ABC-type transport system involved in resistance to organic solvents periplasmic component          | 1.709  | 0.241    |
| DespoDRAFT_01413 | surface lipoprotein   | -1.097 | 0.685    |
| DespoDRAFT_01415 | hypothetical protein  | 1.78   | 0.128    |
| DespoDRAFT_01417 | putative amidohydrolase   | -1.085 | 0.836    |
| DespoDRAFT_01418 | transcriptional regulator   | -1.011 | 0.917    |
| DespoDRAFT_01419 | dsrC: sulfite reductase, dissimilatory-type gamma subunit   | 1.676  | 0.146    |
| DespoDRAFT_01420 | tRNA isopentenyltransferase MiaA  | 1.434  | 0.421    |
| DespoDRAFT_01423 | ABC-type branched-chain amino acid transport system periplasmic component                           | 1.291  | 0.625    |
| DespoDRAFT_01424 | 6-phosphofructokinase   | -1.876 | 0.000688 |
| DespoDRAFT_01425 | KpsF/GutQ family protein  | -1.281 | 0.336    |
| DespoDRAFT_01426 | hypothetical protein  | 2.771  | 0.0852   |
| DespoDRAFT_01427 | aspartate/tyrosine/aromatic aminotransferase  | 2.03   | 0.0248   |
| DespoDRAFT_01428 | pseudouridylate synthase I  | -1.04  | 0.923    |
| DespoDRAFT_01429 | putative quinone oxidoreductase YhdH/YhfP family  | 1.822  | 0.414    |
| DespoDRAFT_01430 | aspA aspartate ammonia-lyase  | -2.312 | 0.0709   |

|                  |   |         |        |
|------------------|---|---------|--------|
| DespoDRAFT_01432 | response regulator with CheY-like receiver domain and winged-helix DNA-binding domain | -1.108  | 0.235  |
| DespoDRAFT_01433 | signal transduction histidine kinase  | -1.313  | 0.276  |
| DespoDRAFT_01434 | periplasmic serine protease Do/DeqQ family  | -1.344  | 0.104  |
| DespoDRAFT_01435 | glutaredoxin-like protein   | -2.097  | 0.135  |
| DespoDRAFT_01437 | parvulin-like peptidyl-prolyl isomerase   | 1.609   | 0.108  |
| DespoDRAFT_01438 | PilZ domain-containing protein  | -1.958  | 0.412  |
| DespoDRAFT_01439 | hypothetical protein  | 1.719   | 0.283  |
| DespoDRAFT_01440 | hypothetical protein  | -1.027  | 0.95   |
| DespoDRAFT_01441 | C-terminal processing peptidase   | -1.397  | 0.223  |
| DespoDRAFT_01442 | ribosome biogenesis GTP-binding protein YlqF  | -1.116  | 0.578  |
| DespoDRAFT_01443 | hypothetical protein  | -1.626  | 0.312  |
| DespoDRAFT_01444 | inositol monophosphatase/fructose-1 6-bisphosphatase family protein                   | -1.132  | 0.71   |
| DespoDRAFT_01445 | soluble lytic murein transglycosylase-like protein                                    | -1.039  | 0.795  |
| DespoDRAFT_01446 | hypothetical protein  | 1.035   | 0.964  |
| DespoDRAFT_01447 | hypothetical protein  | 1.195   | 0.347  |
| DespoDRAFT_01448 | GMP synthase (glutamine-hydrolyzing)  | -1.056  | 0.61   |
| DespoDRAFT_01449 | hypothetical protein  | -1.079  | 0.914  |
| DespoDRAFT_01450 | type I secretion system ABC transporter PrtD family                                   | 2.528   | 0.103  |
| DespoDRAFT_01451 | type I secretion system ABC transporter PrtD family                                   | 3.258   | 0.0265 |
| DespoDRAFT_01452 | ABC-type protease/lipase transport system ATPase and permease component               | 2.056   | 0.128  |
| DespoDRAFT_01453 | type I secretion membrane fusion protein HlyD family                                  | 2.657   | 0.0417 |
| DespoDRAFT_01454 | glycosyltransferase   | 1.674   | 0.196  |
| DespoDRAFT_01455 | hypothetical protein  | -1.426  | 0.152  |
| DespoDRAFT_01456 | hypothetical protein  | -6.736  | 0.0193 |
| DespoDRAFT_01457 | methylase involved in ubiquinone/menaquinone biosynthesis                             | -1.62   | 0.162  |
| DespoDRAFT_01458 | hypothetical protein  | 1.034   | 0.856  |
| DespoDRAFT_01459 | hypothetical protein  | 1.029   | 0.666  |
| DespoDRAFT_01460 | hypothetical protein  | 1.061   | 0.829  |
| DespoDRAFT_01461 | hypothetical protein  | #VALUE! | NaN    |
| DespoDRAFT_01464 | hypothetical protein  | -2.787  | 0.0806 |
| DespoDRAFT_01465 | Protein of unknown function (DUF2442)   | -3.051  | 0.114  |
| DespoDRAFT_01467 | hypothetical protein  | -3.502  | 0.0935 |
| DespoDRAFT_01471 | Protein of unknown function (DUF2442)   | -1.269  | 0.316  |
| DespoDRAFT_01472 | hypothetical protein  | -1.827  | 0.412  |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_01473 | hypothetical protein   | -2.978 | 0.104  |
| DespoDRAFT_01474 | hypothetical protein   | -1.048 | 0.96   |
| DespoDRAFT_01475 | hypothetical protein   | -1.29  | 0.193  |
| DespoDRAFT_01476 | group II intron maturase family protein  | -1.132 | 0.31   |
| DespoDRAFT_01477 | Rhodopirellula transposase   | -11.61 | 0.332  |
| DespoDRAFT_01478 | hypothetical protein   | -3.769 | 0.0564 |
| DespoDRAFT_01479 | hypothetical protein   | -3.768 | 0.0436 |
| DespoDRAFT_01481 | Peptidase M10 serralyisin  | -4.113 | 0.131  |
| DespoDRAFT_01484 | SapC   | 2.57   | 0.0573 |
| DespoDRAFT_01485 | hypothetical protein   | -2.981 | 0.029  |
| DespoDRAFT_01486 | hypothetical protein   | -2.556 | 0.0523 |
| DespoDRAFT_01487 | Matrixin   | -1.91  | 0.173  |
| DespoDRAFT_01488 | hypothetical protein   | -1.609 | 0.0919 |
| DespoDRAFT_01489 | GDP-D-mannose dehydratase  | 2.666  | 0.179  |
| DespoDRAFT_01490 | GDP-mannose 4 6-dehydratase  | 3.018  | 0.0949 |
| DespoDRAFT_01491 | ABC-type polysaccharide/polyol phosphate export system permease component                            | 2.23   | 0.0973 |
| DespoDRAFT_01492 | glycosyltransferase  | 2.255  | 0.31   |
| DespoDRAFT_01493 | ABC-type polysaccharide/polyol phosphate transport system ATPase component                           | 2.452  | 0.0999 |
| DespoDRAFT_01494 | glycosyltransferase  | 1.327  | 0.596  |
| DespoDRAFT_01495 | methylase involved in ubiquinone/menaquinone biosynthesis  | 1.153  | 0.746  |
| DespoDRAFT_01496 | glycosyltransferase  | 2.784  | 0.104  |
| DespoDRAFT_01499 | transposase  | 3.619  | 0.434  |
| DespoDRAFT_01500 | hypothetical protein   | -1.14  | NaN    |
| DespoDRAFT_01501 | hypothetical protein   | -1.719 | 0.488  |
| DespoDRAFT_01502 | hypothetical protein   | -1.357 | 0.576  |
| DespoDRAFT_01503 | Arylsulfotransferase (ASST)  | 1.203  | 0.298  |
| DespoDRAFT_01504 | glycosyl transferase   | -1.045 | 0.922  |
| DespoDRAFT_01505 | putative membrane protein  | -1.347 | 0.88   |
| DespoDRAFT_01506 | hypothetical protein   | -1.156 | 0.828  |
| DespoDRAFT_01507 | putative membrane protein involved in D-alanine export   | 1.415  | 0.702  |
| DespoDRAFT_01508 | hypothetical protein   | 1.456  | 0.186  |
| DespoDRAFT_01509 | translation elongation factor P  | 2.944  | 0.0537 |
| DespoDRAFT_01510 | outer membrane protein   | 1.637  | 0.125  |
| DespoDRAFT_01511 | hypothetical protein   | 2.894  | 0.425  |
| DespoDRAFT_01512 | Ech-hydrogenase-related complex EhrS / Ni Fe-hydrogenase III small subunit                           | 3.696  | 0.0355 |
| DespoDRAFT_01513 | Ni Fe-hydrogenase III large subunit  | 2.69   | 0.0536 |
| DespoDRAFT_01514 | formate hydrogenlyase subunit 3/multisubunit Na <sup>+</sup> /H <sup>+</sup> antiporter MnhD subunit | 2.365  | 0.0878 |
| DespoDRAFT_01515 | hydrogenase 4 membrane component (E)   | 1.727  | 0.119  |

|                  |  |        |         |
|------------------|--|--------|---------|
| DespoDRAFT_01516 | formate hydrogenlyase subunit 4  | 2.567  | 0.284   |
| DespoDRAFT_01517 | formate hydrogenlyase subunit 3/multisubunit Na <sup>+</sup> /H <sup>+</sup> antiporter MnhD subunit | 2.133  | 0.0893  |
| DespoDRAFT_01518 | isoleucine patch superfamily enzyme carbonic anhydrase/acetyltransferase                             | -1.549 | 0.0658  |
| DespoDRAFT_01519 | anaerobic dehydrogenase typically selenocysteine-containing  | 1.036  | 0.881   |
| DespoDRAFT_01520 | potassium uptake protein TrkH family   | -1.209 | 0.331   |
| DespoDRAFT_01521 | K <sup>+</sup> transport system NAD-binding component  | 1.125  | 0.747   |
| DespoDRAFT_01522 | di-/tricarboxylate transporter   | 3.272  | 0.0538  |
| DespoDRAFT_01523 | hypothetical protein   | 1.77   | 0.361   |
| DespoDRAFT_01524 | hypothetical protein   | 1.589  | 0.514   |
| DespoDRAFT_01525 | transcriptional regulator containing PAS AAA-type ATPase   | 1.201  | 0.525   |
| DespoDRAFT_01526 | collagenase-like protease  | -1.036 | 0.867   |
| DespoDRAFT_01527 | cupin domain-containing protein  | -1.006 | 0.986   |
| DespoDRAFT_01528 | hypothetical protein   | 1.581  | 0.256   |
| DespoDRAFT_01529 | hypothetical protein   | -1.173 | 0.54    |
| DespoDRAFT_01530 | putative MccF-like protein (microcin C7 resistance)  | -1.325 | 0.293   |
| DespoDRAFT_01531 | penicillin-binding protein beta-lactamase class C  | -1.241 | 0.29    |
| DespoDRAFT_01532 | cell shape determining protein MreB/Mrl family   | 1.114  | 0.59    |
| DespoDRAFT_01533 | rod shape-determining protein MreC   | 1.744  | 0.235   |
| DespoDRAFT_01534 | hypothetical protein   | -1.049 | 0.948   |
| DespoDRAFT_01535 | penicillin-binding protein 2   | 2.725  | 0.136   |
| DespoDRAFT_01536 | rod shape-determining protein RodA   | 2.34   | 0.26    |
| DespoDRAFT_01537 | F <sub>0</sub> F <sub>1</sub> -type ATP synthase beta subunit  | 2.759  | 0.0578  |
| DespoDRAFT_01538 | ATP synthase F <sub>0</sub> subunit b  | 2.432  | 0.00692 |
| DespoDRAFT_01539 | ATP synthase F <sub>1</sub> delta subunit  | 2.823  | 0.0274  |
| DespoDRAFT_01540 | proton translocating ATP synthase F <sub>1</sub> alpha subunit                                       | 2.376  | 0.0449  |
| DespoDRAFT_01541 | ATP synthase F <sub>1</sub> gamma subunit  | 2.627  | 0.0255  |
| DespoDRAFT_01542 | ATP synthase F <sub>1</sub> beta subunit   | 3.385  | 0.0607  |
| DespoDRAFT_01543 | ATP synthase F <sub>1</sub> epsilon subunit  | 2.708  | 0.0464  |
| DespoDRAFT_01544 | N-acetylglucosamine-1-phosphate uridylyltransferase/acetyltransferase                                | 1.635  | 0.126   |
| DespoDRAFT_01545 | hypothetical protein   | -1.29  | 0.286   |
| DespoDRAFT_01546 | Cell division protein ZapA   | -1.044 | 0.959   |
| DespoDRAFT_01547 | hypothetical protein   | 1.633  | 0.165   |
| DespoDRAFT_01548 | tyrosyl-tRNA synthetase  | 1.69   | 0.0496  |
| DespoDRAFT_01555 | phosphopantetheine-containing protein  | 1.322  | 0.568   |



|                  |  |        |         |
|------------------|--|--------|---------|
| DespoDRAFT_01556 | 3-oxoacyl-(acyl-carrier-protein) synthase  | 1.228  | 0.54    |
| DespoDRAFT_01557 | Fe-S oxidoreductase  | -1.046 | 0.963   |
| DespoDRAFT_01558 | hypothetical protein   | -1.206 | 0.861   |
| DespoDRAFT_01559 | outer membrane lipoprotein-sorting protein   | -1.625 | 0.307   |
| DespoDRAFT_01560 | dehydrogenase of unknown specificity   | 1.043  | 0.909   |
| DespoDRAFT_01561 | hypothetical protein   | -1.388 | 0.655   |
| DespoDRAFT_01562 | hypothetical protein   | 1.446  | 0.567   |
| DespoDRAFT_01563 | Ni Fe-hydrogenase I large subunit  | -1.155 | 0.732   |
| DespoDRAFT_01564 | hydrogenase (NiFe) small subunit HydA  | -2.541 | 0.159   |
| DespoDRAFT_01565 | methyl-accepting chemotaxis protein  | -1.083 | 0.926   |
| DespoDRAFT_01566 | hypothetical protein   | -2.466 | 0.0545  |
| DespoDRAFT_01567 | ABC-type transport system involved in Fe-S cluster assembly permease component     | -1.269 | 0.347   |
| DespoDRAFT_01568 | ABC-type transport system involved in Fe-S cluster assembly ATPase component       | -1.191 | 0.23    |
| DespoDRAFT_01569 | oligopeptide/dipeptide ABC transporter ATP-binding protein                         | 1.408  | 0.619   |
| DespoDRAFT_01570 | ABC-type dipeptide/oligopeptide/nickel transport system permease component         | 2.197  | NaN     |
| DespoDRAFT_01571 | ABC-type dipeptide/oligopeptide/nickel transport system permease component         | 2.055  | 0.478   |
| DespoDRAFT_01572 | ABC-type dipeptide transport system periplasmic component                          | 18.241 | 0.0948  |
| DespoDRAFT_01573 | methylase involved in ubiquinone/menaquinone biosynthesis                          | 4.843  | 0.17    |
| DespoDRAFT_01574 | outer membrane receptor protein  | 6.213  | 0.102   |
| DespoDRAFT_01575 | hypothetical protein   | 1.584  | NaN     |
| DespoDRAFT_01576 | TonB family protein  | 1.401  | 0.791   |
| DespoDRAFT_01577 | biopolymer transport protein   | -1.414 | NaN     |
| DespoDRAFT_01578 | biopolymer transport protein   | -1.155 | 0.916   |
| DespoDRAFT_01579 | biopolymer transport protein   | 4.083  | 0.36    |
| DespoDRAFT_01580 | Protein of unknown function (DUF3450)  | -1.095 | NaN     |
| DespoDRAFT_01581 | NhaP-type Na <sup>+</sup> (K <sup>+</sup> )/H <sup>+</sup> antiporter              | -1.437 | 0.452   |
| DespoDRAFT_01582 | superoxide dismutase   | -2.029 | 0.0407  |
| DespoDRAFT_01583 | universal stress protein UspA-like protein   | -2.789 | 0.00982 |
| DespoDRAFT_01584 | diaminopimelate decarboxylase  | -2.405 | 0.051   |
| DespoDRAFT_01585 | biotin carboxylase   | -2.51  | 0.0831  |
| DespoDRAFT_01586 | hypothetical protein   | -1.999 | 0.0499  |
| DespoDRAFT_01587 | hypothetical protein   | -2.144 | 0.133   |
| DespoDRAFT_01588 | hypothetical protein   | -2.063 | 0.148   |
| DespoDRAFT_01589 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains | 1.11   | 0.734   |
| DespoDRAFT_01590 | hypothetical protein   | -1.196 | 0.62    |
| DespoDRAFT_01591 | DnaK suppressor protein  | 1.596  | 0.249   |

|                  |  |        |         |
|------------------|--|--------|---------|
| DespoDRAFT_01592 | hypothetical protein   | 1.312  | 0.17    |
| DespoDRAFT_01593 | coenzyme F420-reducing hydrogenase delta subunit                       | 1.448  | 0.202   |
| DespoDRAFT_01594 | FAD/FMN-dependent dehydrogenase  | 1.204  | 0.39    |
| DespoDRAFT_01598 | hypothetical protein   | 1.172  | 0.834   |
| DespoDRAFT_01599 | hypothetical protein   | -2.568 | NaN     |
| DespoDRAFT_01600 | hypothetical protein   | -1.336 | 0.135   |
| DespoDRAFT_01601 | outer membrane protein assembly complex YaeT protein                   | -1.014 | 0.959   |
| DespoDRAFT_01602 | universal stress protein UspA-like protein                             | 1.145  | 0.79    |
| DespoDRAFT_01603 | glutamyl- or glutaminyl-tRNA synthetase                                | 1.173  | 0.354   |
| DespoDRAFT_01604 | PilZ domain-containing protein   | 1.23   | 0.512   |
| DespoDRAFT_01605 | DNA topoisomerase I bacterial  | 2.417  | 0.00846 |
| DespoDRAFT_01606 | DNA protecting protein DprA  | 1.903  | 0.449   |
| DespoDRAFT_01607 | tol-pal system protein YbgF  | 2.134  | 0.28    |
| DespoDRAFT_01608 | preprotein translocase subunit SecF                                    | 3.038  | 0.0465  |
| DespoDRAFT_01609 | hypothetical protein   | 1.777  | 0.133   |
| DespoDRAFT_01610 | diaminopimelate decarboxylase  | 1.772  | 0.0925  |
| DespoDRAFT_01611 | asparagine synthase (glutamine-hydrolyzing)                            | 1.405  | 0.128   |
| DespoDRAFT_01612 | acyltransferase family protein   | 1.432  | 0.206   |
| DespoDRAFT_01613 | PEP-CTERM/exosortase 1-associated glycosyltransferase Daro_2409 family | 1.092  | 0.79    |
| DespoDRAFT_01614 | transposase family protein   | -1.183 | 0.672   |
| DespoDRAFT_01615 | putative methicillin resistance protein                                | -1.104 | 0.783   |
| DespoDRAFT_01616 | hypothetical protein   | -2.141 | 0.169   |
| DespoDRAFT_01617 | hypothetical protein   | -1.523 | 0.236   |
| DespoDRAFT_01618 | diaminopimelate decarboxylase  | -1.135 | 0.783   |
| DespoDRAFT_01619 | asparagine synthase (glutamine-hydrolyzing)                            | -1.087 | 0.61    |
| DespoDRAFT_01621 | acyltransferase family protein   | -1.001 | 0.998   |
| DespoDRAFT_01622 | PEP-CTERM/exosortase 1-associated glycosyltransferase Daro_2409 family | -3.081 | 0.13    |
| DespoDRAFT_01623 | transposase family protein   | -1.5   | 0.663   |
| DespoDRAFT_01624 | putative methicillin resistance protein                                | 1.749  | 0.48    |
| DespoDRAFT_01625 | hypothetical protein   | 1.186  | 0.653   |
| DespoDRAFT_01626 | hypothetical protein   | -1.581 | 0.348   |
| DespoDRAFT_01629 | diaminopimelate decarboxylase  | -3.195 | 0.347   |
| DespoDRAFT_01631 | asparagine synthase (glutamine-hydrolyzing)                            | -1.606 | 0.0502  |
| DespoDRAFT_01632 | acyltransferase family protein   | -2.546 | 0.112   |
| DespoDRAFT_01633 | PEP-CTERM/exosortase 1-associated glycosyltransferase Daro_2409 family | -1.726 | 0.0638  |
| DespoDRAFT_01634 | transposase family protein   | -2.173 | 0.25    |
| DespoDRAFT_01635 | putative methicillin resistance protein                                | -1.909 | 0.0439  |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_01636 | hypothetical protein   | -2.872 | 0.139  |
| DespoDRAFT_01637 | hypothetical protein   | -1.687 | 0.128  |
| DespoDRAFT_01638 | diaminopimelate decarboxylase  | -1.638 | 0.199  |
| DespoDRAFT_01639 | asparagine synthase (glutamine-hydrolyzing)                            | -1.251 | 0.291  |
| DespoDRAFT_01640 | acyltransferase family protein   | -1.664 | 0.125  |
| DespoDRAFT_01641 | PEP-CTERM/exosortase 1-associated glycosyltransferase Daro_2409 family | -2.219 | 0.0657 |
| DespoDRAFT_01642 | transposase family protein   | -2.193 | 0.131  |
| DespoDRAFT_01643 | putative methicillin resistance protein                                | -1.42  | 0.1    |
| DespoDRAFT_01644 | hypothetical protein   | -1.279 | 0.0393 |
| DespoDRAFT_01645 | aspA asparagine synthase   | -1.064 | 0.669  |
| DespoDRAFT_01646 | lipid A core-O-antigen ligase-like enzyme                              | -1.362 | 0.206  |
| DespoDRAFT_01647 | glycosyltransferase  | -1.334 | 0.412  |
| DespoDRAFT_01648 | putative xylanase/chitin deacetylase                                   | -1.372 | 0.203  |
| DespoDRAFT_01649 | hypothetical protein   | -1.097 | 0.522  |
| DespoDRAFT_01650 | sulfotransferase family protein  | 1.275  | 0.555  |
| DespoDRAFT_01651 | glycosyl transferase   | -2.802 | 0.141  |
| DespoDRAFT_01652 | exopolysaccharide biosynthesis protein                                 | -1.714 | 0.219  |
| DespoDRAFT_01653 | membrane protein involved in the export of O-antigen and teichoic acid | -1.263 | 0.61   |
| DespoDRAFT_01654 | hypothetical protein   | -1.004 | 0.99   |
| DespoDRAFT_01655 | protein involved in cellulose biosynthesis (CelD)                      | 1.127  | 0.661  |
| DespoDRAFT_01656 | hypothetical protein   | 1.101  | 0.605  |
| DespoDRAFT_01657 | hypothetical protein   | -1.057 | 0.783  |
| DespoDRAFT_01658 | diaminopimelate decarboxylase  | -1.238 | 0.182  |
| DespoDRAFT_01659 | asparagine synthase (glutamine-hydrolyzing)                            | -1.241 | 0.361  |
| DespoDRAFT_01660 | acyltransferase family protein   | -1.302 | 0.498  |
| DespoDRAFT_01661 | PEP-CTERM/exosortase 1-associated glycosyltransferase Daro_2409 family | -1.477 | 0.157  |
| DespoDRAFT_01663 | putative methicillin resistance protein                                | -1.17  | 0.656  |
| DespoDRAFT_01664 | hypothetical protein   | -1.255 | 0.236  |
| DespoDRAFT_01669 | hypothetical protein   | -1.307 | 0.568  |
| DespoDRAFT_01670 | hypothetical protein   | -1.399 | 0.383  |
| DespoDRAFT_01671 | hypothetical protein   | 1.183  | 0.63   |
| DespoDRAFT_01672 | hypothetical protein   | -1.457 | 0.083  |
| DespoDRAFT_01673 | hypothetical protein   | -1.859 | 0.128  |
| DespoDRAFT_01674 | putative nucleotidyltransferase  | -2.302 | 0.269  |
| DespoDRAFT_01676 | putative transcriptional regulator with HTH domain                     | -1.844 | 0.0897 |
| DespoDRAFT_01677 | nucleotidyltransferase substrate binding protein HI0074 family         | 1.128  | 0.855  |
| DespoDRAFT_01678 | nucleotidyltransferase family protein                                  | -1.328 | 0.369  |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_01679 | putative transcriptional regulator with HTH domain   | -1.159 | 0.846  |
| DespoDRAFT_01680 | hypothetical protein   | 1.6    | 0.596  |
| DespoDRAFT_01681 | hypothetical protein   | 1.448  | 0.468  |
| DespoDRAFT_01682 | UDP-N-acetylglucosamine 2-epimerase  | -1.075 | 0.638  |
| DespoDRAFT_01683 | nucleotide sugar dehydrogenase   | 1.345  | 0.185  |
| DespoDRAFT_01684 | polysaccharide deactylase family protein PEP-CTERM locus subfamily   | -1.346 | 0.62   |
| DespoDRAFT_01685 | eight transmembrane protein EpsH putative exosortase   | -1.454 | 0.262  |
| DespoDRAFT_01686 | EpsI family protein  | -1.967 | 0.0636 |
| DespoDRAFT_01687 | hypothetical protein   | -1.619 | 0.156  |
| DespoDRAFT_01688 | periplasmic protein involved in polysaccharide export  | -1.186 | 0.325  |
| DespoDRAFT_01689 | sugar transferase PEP-CTERM system associated/exopolysaccharide biosynthesis polyprenyl glycosylphosphotransferase | -1.446 | 0.461  |
| DespoDRAFT_01690 | capsular exopolysaccharide biosynthesis protein  | 1.086  | 0.922  |
| DespoDRAFT_01691 | uncharacterized protein involved in exopolysaccharide biosynthesis   | -1.079 | 0.774  |
| DespoDRAFT_01692 | nucleoside-diphosphate-sugar epimerase   | -1.051 | 0.833  |
| DespoDRAFT_01693 | CAAX amino terminal protease family  | -1.535 | 0.498  |
| DespoDRAFT_01694 | type II secretory pathway component ExeA (predicted ATPase)  | -1.293 | 0.655  |
| DespoDRAFT_01695 | hypothetical protein   | -1.592 | 0.314  |
| DespoDRAFT_01696 | hypothetical protein   | -1.218 | 0.646  |
| DespoDRAFT_01697 | Lhr-like helicase  | -1.175 | 0.514  |
| DespoDRAFT_01698 | Protein of unknown function (DUF2791)  | 1.075  | 0.545  |
| DespoDRAFT_01699 | ATPase   | 1.228  | 0.107  |
| DespoDRAFT_01700 | hypothetical protein   | 2.828  | 0.0658 |
| DespoDRAFT_01701 | lysophospholipase L1-like esterase   | -1.189 | 0.534  |
| DespoDRAFT_01702 | ABC-type antimicrobial peptide transport system ATPase component   | 3.266  | 0.559  |
| DespoDRAFT_01703 | putative ABC-type transport system involved in lysophospholipase L1 biosynthesis permease component                | 1.443  | 0.499  |
| DespoDRAFT_01704 | hypothetical protein   | 1.019  | 0.886  |
| DespoDRAFT_01705 | uncharacterized protein involved in tolerance to divalent cations  | -1.051 | 0.871  |
| DespoDRAFT_01706 | hypothetical protein   | -1.697 | 0.154  |
| DespoDRAFT_01707 | UDP-glucose-4-epimerase  | 1.003  | 0.987  |
| DespoDRAFT_01708 | hypothetical protein   | -1.83  | 0.143  |
| DespoDRAFT_01709 | hypothetical protein   | -1.853 | 0.199  |
| DespoDRAFT_01710 | transcriptional regulator  | -1.614 | 0.259  |

|                  |   |        |        |
|------------------|---|--------|--------|
| DespoDRAFT_01711 | Flagellar basal body-associated protein FliL                            | -1.516 | 0.129  |
| DespoDRAFT_01712 | thiamine pyrophosphokinase  | -1.161 | 0.651  |
| DespoDRAFT_01713 | putative permease   | 2.129  | 0.0887 |
| DespoDRAFT_01714 | putative permease   | 1.573  | 0.386  |
| DespoDRAFT_01715 | 3-deoxy-D-manno-octulosonic-acid transferase                            | 2.574  | 0.0756 |
| DespoDRAFT_01716 | tetraacyldisaccharide 4"-kinase   | 1.856  | 0.141  |
| DespoDRAFT_01717 | Lauroyl/myristoyl acyltransferase                                       | 1.061  | 0.808  |
| DespoDRAFT_01718 | lipopolysaccharide heptosyltransferase II                               | 1.441  | 0.251  |
| DespoDRAFT_01719 | ADP-heptose:LPS heptosyltransferase                                     | 1.917  | 0.198  |
| DespoDRAFT_01720 | glycosyl transferase  | 1.072  | 0.931  |
| DespoDRAFT_01721 | putative glycosyltransferase  | -1.587 | 0.174  |
| DespoDRAFT_01722 | hypothetical protein  | -1.398 | 0.467  |
| DespoDRAFT_01723 | lipid A core-O-antigen ligase-like enzyme                               | -1.505 | 0.425  |
| DespoDRAFT_01724 | glycosyltransferase   | -1.045 | 0.949  |
| DespoDRAFT_01725 | hypothetical protein  | -1.507 | 0.255  |
| DespoDRAFT_01726 | glycosyltransferase   | -1.186 | 0.506  |
| DespoDRAFT_01727 | glycosyltransferase   | -1.086 | 0.847  |
| DespoDRAFT_01728 | 3-deoxy-D-manno-octulosonate cytidyltransferase                         | -1.091 | 0.424  |
| DespoDRAFT_01729 | alcohol dehydrogenase class IV  | -1.149 | 0.262  |
| DespoDRAFT_01730 | putative PLP-dependent enzyme possibly involved in cell wall biogenesis | 1.351  | 0.101  |
| DespoDRAFT_01731 | Fe-S oxidoreductase   | -1.911 | 0.0484 |
| DespoDRAFT_01732 | putative oxygen-independent coproporphyrinogen III oxidase              | 1.388  | 0.485  |
| DespoDRAFT_01733 | selenocysteine-specific elongation factor SelB                          | -1.578 | 0.148  |
| DespoDRAFT_01734 | hypothetical protein  | -1.257 | 0.602  |
| DespoDRAFT_01736 | cytidylate kinase   | -1.265 | 0.0672 |
| DespoDRAFT_01738 | inorganic pyrophosphatase/exopolyphosphatase                            | 1.913  | 0.101  |
| DespoDRAFT_01739 | acyl-CoA synthetase (AMP-forming)/AMP-acid ligase II                    | -1.544 | 0.322  |
| DespoDRAFT_01740 | cobalt ABC transporter permease protein CbiQ                            | -1.291 | 0.653  |
| DespoDRAFT_01741 | ABC-type cobalt transport system ATPase component                       | 1.025  | 0.985  |
| DespoDRAFT_01742 | phosphoserine aminotransferase  | 6.266  | 0.0313 |
| DespoDRAFT_01743 | D-3-phosphoglycerate dehydrogenase                                      | 4.408  | 0.0317 |
| DespoDRAFT_01744 | rare lipoprotein A  | 2.36   | 0.0466 |
| DespoDRAFT_01745 | Transglycosylase  | 2.177  | 0.165  |
| DespoDRAFT_01746 | hypothetical protein  | 1.995  | 0.372  |
| DespoDRAFT_01747 | hypothetical protein  | -1.785 | 0.0145 |
| DespoDRAFT_01748 | N-carbamoylputrescine amidase   | -1.424 | 0.106  |

|                  |   |        |        |
|------------------|---|--------|--------|
| DespoDRAFT_01749 | peptidylarginine deiminase-like enzyme                                | 1.284  | 0.156  |
| DespoDRAFT_01750 | spermidine/putrescine-binding periplasmic protein                     | 3.588  | 0.0635 |
| DespoDRAFT_01751 | ABC-type spermidine/putrescine transport system permease component II | 1.196  | 0.867  |
| DespoDRAFT_01752 | ABC-type spermidine/putrescine transport system permease component I  | 2.356  | 0.319  |
| DespoDRAFT_01753 | CysA: sulfate/thiosulfate import ATP-binding protein CysA             | 1.96   | 0.59   |
| DespoDRAFT_01754 | transcriptional regulator   | 2.065  | 0.619  |
| DespoDRAFT_01755 | SH3 domain protein  | 1.439  | 0.0862 |
| DespoDRAFT_01756 | L-aspartate oxidase   | 1.187  | 0.32   |
| DespoDRAFT_01757 | Phosphoglucomutase  | 1.151  | 0.52   |
| DespoDRAFT_01758 | putative periplasmic lipoprotein (DUF2279)                            | -1.476 | 0.202  |
| DespoDRAFT_01759 | ribonucleoside-diphosphate reductase adenosylcobalamin-dependent      | 1.021  | 0.853  |
| DespoDRAFT_01760 | carbonic anhydrase  | 1.234  | 0.502  |
| DespoDRAFT_01761 | hypothetical protein  | -1.609 | 0.515  |
| DespoDRAFT_01762 | TIR domain-containing protein   | -1.633 | 0.108  |
| DespoDRAFT_01763 | MoxR-like ATPase  | 1.088  | 0.591  |
| DespoDRAFT_01764 | hypothetical protein  | 1.248  | 0.658  |
| DespoDRAFT_01766 | Retron-type reverse transcriptase                                     | 1.597  | 0.622  |
| DespoDRAFT_01767 | hypothetical protein  | -1.203 | 0.14   |
| DespoDRAFT_01768 | hypothetical protein  | -1.314 | 0.0852 |
| DespoDRAFT_01769 | cobalamin biosynthesis CbiM protein                                   | -2.131 | 0.173  |
| DespoDRAFT_01770 | ABC-type Co <sup>2+</sup> transport system permease component         | -3.693 | 0.151  |
| DespoDRAFT_01771 | ABC-type Co <sup>2+</sup> transport system periplasmic component      | -4.297 | 0.068  |
| DespoDRAFT_01772 | methyltransferase cyclopropane fatty acid synthase                    | -3.832 | 0.0637 |
| DespoDRAFT_01773 | acyl-CoA synthetase/AMP-acid ligase                                   | 2.244  | 0.0149 |
| DespoDRAFT_01774 | 1-acyl-sn-glycerol-3-phosphate acyltransferase                        | 1.792  | 0.449  |
| DespoDRAFT_01775 | hypothetical protein  | -1.006 | 0.993  |
| DespoDRAFT_01776 | putative GTPase   | -1.442 | 0.0728 |
| DespoDRAFT_01777 | hypothetical protein  | -1.565 | 0.183  |
| DespoDRAFT_01778 | hypothetical protein  | -1.931 | 0.173  |
| DespoDRAFT_01779 | hypothetical protein  | -2.259 | 0.227  |
| DespoDRAFT_01780 | hypothetical protein  | -1.328 | 0.428  |
| DespoDRAFT_01781 | hypothetical protein  | -1.823 | 0.273  |
| DespoDRAFT_01782 | hypothetical protein  | -1.587 | 0.229  |
| DespoDRAFT_01783 | excinuclease ABC A subunit  | -1.206 | 0.442  |
| DespoDRAFT_01784 | 4-hydroxythreonine-4-phosphate dehydrogenase                          | -1.142 | 0.463  |

|                  |  |         |        |
|------------------|--|---------|--------|
| DespoDRAFT_01785 | chromosomal replication initiator protein DnaA                                       | 1.762   | 0.141  |
| DespoDRAFT_01786 | hypothetical protein   | 1.054   | 0.944  |
| DespoDRAFT_01787 | GTP-binding protein HflX   | 2.157   | 0.199  |
| DespoDRAFT_01788 | replicative DNA helicase   | 1.797   | 0.0451 |
| DespoDRAFT_01789 | ribosomal protein L9   | 3.111   | 0.0659 |
| DespoDRAFT_01790 | putative membrane protein  | 4.514   | 0.0438 |
| DespoDRAFT_01791 | ribosomal protein S18  | 3.823   | 0.0582 |
| DespoDRAFT_01792 | ribosomal protein S6   | 4.357   | 0.0338 |
| DespoDRAFT_01793 | TIGR02688 family protein   | -1.443  | 0.774  |
| DespoDRAFT_01796 | hypothetical protein   | 1.404   | 0.205  |
| DespoDRAFT_01797 | putative ATPase  | 1.286   | 0.614  |
| DespoDRAFT_01798 | Eco57I restriction endonuclease  | 1.054   | 0.73   |
| DespoDRAFT_01799 | protein of unknown function (DUF1788)  | -1.214  | 0.848  |
| DespoDRAFT_01800 | Putative inner membrane protein (DUF1819)  | 1.045   | 0.948  |
| DespoDRAFT_01801 | hypothetical protein   | 1.913   | 0.109  |
| DespoDRAFT_01802 | leucyl-tRNA synthetase   | 2.518   | 0.0315 |
| DespoDRAFT_01803 | hypothetical protein   | 2.059   | 0.193  |
| DespoDRAFT_01804 | ribosomal protein S20  | 1.617   | 0.505  |
| DespoDRAFT_01805 | hypothetical protein   | -1.013  | 0.984  |
| DespoDRAFT_01806 | septum formation initiator   | -1.288  | 0.191  |
| DespoDRAFT_01807 | hypothetical protein   | -1.872  | 0.0466 |
| DespoDRAFT_01808 | hypothetical protein   | -1.482  | 0.273  |
| DespoDRAFT_01810 | Uncharacterized protein family (UPF0153)   | 1.096   | 0.634  |
| DespoDRAFT_01811 | hypothetical protein   | 2.59    | 0.275  |
| DespoDRAFT_01812 | LysM domain-containing protein   | 2.07    | 0.159  |
| DespoDRAFT_01813 | phosphoribosylanthranilate isomerase   | 2.174   | 0.0634 |
| DespoDRAFT_01814 | Indole-3-glycerol phosphate synthase   | 2.283   | 0.219  |
| DespoDRAFT_01815 | anthranilate phosphoribosyltransferase   | 2.108   | 0.0338 |
| DespoDRAFT_01816 | glutamine amidotransferase of anthranilate synthase or aminodeoxychorismate synthase | 3.12    | 0.0573 |
| DespoDRAFT_01817 | anthranilate/para-aminobenzoate synthase component I                                 | 2.897   | 0.0682 |
| DespoDRAFT_01818 | hypothetical protein   | 1.767   | 0.47   |
| DespoDRAFT_01819 | hypothetical protein   | #VALUE! | NaN    |
| DespoDRAFT_01820 | Fe-S oxidoreductase  | 1.345   | 0.57   |
| DespoDRAFT_01821 | competence/damage-inducible protein CinA-like protein                                | -1.112  | 0.69   |
| DespoDRAFT_01822 | outer membrane protein/peptidoglycan-associated (lipo)protein                        | -1.151  | 0.343  |
| DespoDRAFT_01823 | prolyl oligopeptidase family protein   | -1.699  | 0.272  |
| DespoDRAFT_01824 | 23S rRNA (uracil-5-)-methyltransferase RumA  | 3.722   | 0.225  |
| DespoDRAFT_01825 | acetyl-CoA hydrolase   | -2.726  | 0.131  |

|                  |   |        |         |
|------------------|---|--------|---------|
| DespoDRAFT_01826 | hypothetical protein  | -4.427 | 0.102   |
| DespoDRAFT_01827 | 3, 4-dihydroxy-2-butanone 4-phosphate synthase                                  | -1.272 | 0.692   |
| DespoDRAFT_01828 | hypothetical protein  | 1.242  | 0.819   |
| DespoDRAFT_01829 | hypothetical protein  | -1.253 | 0.818   |
| DespoDRAFT_01830 | type II secretory pathway, component PulC                                       | -1.491 | 0.583   |
| DespoDRAFT_01831 | hypothetical protein  | -2.144 | 0.18    |
| DespoDRAFT_01832 | hypothetical protein  | -2.758 | 0.172   |
| DespoDRAFT_01833 | ATPase involved in chromosome partitioning                                      | -2.681 | 0.116   |
| DespoDRAFT_01834 | hypothetical protein  | -2.965 | 0.305   |
| DespoDRAFT_01835 | P-type ATPase translocating   | -2.347 | 0.0242  |
| DespoDRAFT_01836 | universal stress protein UspA-like protein                                      | -2.353 | 0.111   |
| DespoDRAFT_01837 | molybdopterin biosynthesis enzyme   | 1.156  | 0.782   |
| DespoDRAFT_01840 | aerobic-type carbon monoxide dehydrogenase large subunit CoxL/CutL-like protein | -1.532 | 0.00982 |
| DespoDRAFT_01842 | tyrosine recombinase XerD   | -1.632 | 0.0725  |
| DespoDRAFT_01843 | transcription-repair coupling factor Mfd  | 2.647  | 0.128   |
| DespoDRAFT_01845 | soluble lytic murein transglycosylase-like protein                              | -1.198 | 0.209   |
| DespoDRAFT_01847 | hypothetical protein  | -1.956 | 0.234   |
| DespoDRAFT_01848 | sugar phosphate permease  | -1.474 | 0.236   |
| DespoDRAFT_01849 | putative divalent heavy-metal cations transporter                               | 1.631  | 0.153   |
| DespoDRAFT_01850 | putative dithiol-disulfide isomerase involved in polyketide biosynthesis        | -1.44  | 0.349   |
| DespoDRAFT_01851 | cupin domain-containing protein   | 2.114  | 0.112   |
| DespoDRAFT_01852 | putative membrane protein   | 1.894  | 0.381   |
| DespoDRAFT_01853 | ubiquinone/menaquinone biosynthesis methyltransferase                           | 2.123  | 0.0465  |
| DespoDRAFT_01854 | chaperone protein DnaJ  | 1.513  | 0.0945  |
| DespoDRAFT_01855 | queuosine biosynthesis protein QueD   | 1.088  | 0.721   |
| DespoDRAFT_01856 | FAD-dependent dehydrogenase   | -1.016 | 0.963   |
| DespoDRAFT_01857 | hypothetical protein  | 1.692  | 0.535   |
| DespoDRAFT_01858 | molecular chaperone   | 1.561  | 0.0437  |
| DespoDRAFT_01859 | hypothetical protein  | -1.154 | 0.317   |
| DespoDRAFT_01860 | hypothetical protein  | 1.488  | 0.0729  |
| DespoDRAFT_01861 | hypothetical protein  | 1.962  | 0.264   |
| DespoDRAFT_01862 | GrpE protein  | 2.113  | 0.148   |
| DespoDRAFT_01863 | hypothetical protein  | 2.248  | 0.138   |
| DespoDRAFT_01864 | membrane protein AbrB duplication   | 2.478  | 0.105   |
| DespoDRAFT_01865 | ATPase component of ABC transporters with duplicated ATPase domain              | 1.052  | 0.785   |
| DespoDRAFT_01866 | hypothetical protein  | 1.222  | 0.851   |



|                  |  |         |        |
|------------------|--|---------|--------|
| DespoDRAFT_01867 | chloride channel protein EriC  | 1.167   | 0.663  |
| DespoDRAFT_01868 | DNA-binding protein excisionase family   | -1.218  | 0.0828 |
| DespoDRAFT_01869 | hypothetical protein   | -2.201  | 0.489  |
| DespoDRAFT_01870 | growth inhibitor   | -1.295  | 0.0675 |
| DespoDRAFT_01871 | hypothetical protein   | 1.308   | 0.475  |
| DespoDRAFT_01872 | DNA modification methylase   | 2.152   | 0.139  |
| DespoDRAFT_01873 | Restriction endonuclease XhoI  | 1.601   | 0.239  |
| DespoDRAFT_01874 | Lhr-like helicase  | 1.457   | 0.498  |
| DespoDRAFT_01875 | Protein of unknown function (DUF2791)  | 1.317   | 0.505  |
| DespoDRAFT_01876 | tellurite resistance protein   | -1.108  | 0.816  |
| DespoDRAFT_01877 | hypothetical protein   | -1.406  | 0.113  |
| DespoDRAFT_01878 | hypothetical protein   | -1.488  | 0.0951 |
| DespoDRAFT_01879 | hypothetical protein   | -1.5    | 0.468  |
| DespoDRAFT_01880 | putative signal-transduction protein containing cAMP-binding and CBS domains             | -2.259  | 0.102  |
| DespoDRAFT_01881 | hypothetical protein   | -1.113  | 0.903  |
| DespoDRAFT_01882 | nitroreductase   | -1.377  | 0.633  |
| DespoDRAFT_01883 | hypothetical protein   | #VALUE! | NaN    |
| DespoDRAFT_01884 | hypothetical protein   | #VALUE! | NaN    |
| DespoDRAFT_01887 | putative addiction module antidote protein   | -1.231  | 0.475  |
| DespoDRAFT_01890 | hypothetical protein   | -1.636  | 0.291  |
| DespoDRAFT_01891 | hypothetical protein   | -1.875  | 0.151  |
| DespoDRAFT_01892 | growth inhibitor   | -2.734  | 0.15   |
| DespoDRAFT_01893 | hypothetical protein   | -2.869  | 0.134  |
| DespoDRAFT_01894 | putative small protein   | -1.591  | 0.295  |
| DespoDRAFT_01895 | phage-related protein  | -1.543  | 0.104  |
| DespoDRAFT_01896 | hypothetical protein   | -1.553  | 0.632  |
| DespoDRAFT_01897 | PEP-CTERM putative exosortase interaction domain-containing protein                      | -1.332  | 0.677  |
| DespoDRAFT_01898 | methylase involved in ubiquinone/menaquinone biosynthesis                                | -1.39   | 0.489  |
| DespoDRAFT_01899 | hypothetical protein   | 1.19    | 0.651  |
| DespoDRAFT_01900 | glycosyl transferase UDP-glucuronosyltransferase   | 1.19    | 0.832  |
| DespoDRAFT_01901 | hypothetical protein   | -1.221  | 0.731  |
| DespoDRAFT_01902 | hypothetical protein   | -1.498  | 0.53   |
| DespoDRAFT_01903 | ABC-type transport system, involved in lipoprotein release permease component            | -2.396  | 0.148  |
| DespoDRAFT_01904 | ABC-type antimicrobial peptide transport system, ATPase component                        | -3.183  | 0.0381 |
| DespoDRAFT_01905 | hypothetical protein   | -2.859  | 0.0964 |
| DespoDRAFT_01906 | dinucleotide-utilizing enzyme possibly involved in molybdopterin or thiamin biosynthesis | -2.775  | 0.0637 |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_01907 | putative PEP-CTERM/exosortase system-associated acyltransferase                    | -2.638 | 0.0831 |
| DespoDRAFT_01908 | Protein of unknown function (DUF1329)  | -2.68  | 0.231  |
| DespoDRAFT_01909 | hypothetical protein   | -2.362 | 0.127  |
| DespoDRAFT_01910 | hypothetical protein   | -1.727 | 0.148  |
| DespoDRAFT_01911 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains | -1.502 | 0.453  |
| DespoDRAFT_01912 | histidine kinase   | -1.526 | 0.471  |
| DespoDRAFT_01913 | hypothetical protein   | -3.532 | 0.125  |
| DespoDRAFT_01914 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains | -3.323 | 0.0696 |
| DespoDRAFT_01915 | chemotaxis protein   | -3.243 | 0.0339 |
| DespoDRAFT_01916 | chemotaxis protein histidine kinase-like protein                                   | -3.236 | 0.1    |
| DespoDRAFT_01917 | 3-deoxy-7-phosphoheptulonate synthase class II                                     | -1.136 | 0.0829 |
| DespoDRAFT_01918 | putative amidohydrolase  | -1.384 | 0.128  |
| DespoDRAFT_01919 | D-heptose-1-phosphate adenylyltransferase  | -1.488 | 0.0659 |
| DespoDRAFT_01920 | uncharacterized protein YfiH family  | -1.27  | 0.476  |
| DespoDRAFT_01921 | selenium donor protein   | -1.407 | 0.285  |
| DespoDRAFT_01922 | Putative F0F1-ATPase subunit   | 1.41   | 0.445  |
| DespoDRAFT_01923 | ATP synthase I chain   | 1.845  | 0.26   |
| DespoDRAFT_01924 | F0F1-type ATP synthase alpha subunit   | 2.137  | 0.0807 |
| DespoDRAFT_01925 | ATP synthase F0 subunit c  | 1.263  | 0.435  |
| DespoDRAFT_01926 | hypothetical protein   | -1.376 | 0.167  |
| DespoDRAFT_01927 | ATPase involved in chromosome partitioning   | -1.039 | 0.944  |
| DespoDRAFT_01928 | HAMP domain-containing protein histidine kinase GAF domain-containing protein      | -1.493 | 0.478  |
| DespoDRAFT_01929 | di-/tricarboxylate transporter   | -1.768 | 0.324  |
| DespoDRAFT_01930 | ACT domain-containing protein  | 1.546  | 0.148  |
| DespoDRAFT_01931 | coenzyme F390 synthetase   | 2.352  | 0.0662 |
| DespoDRAFT_01932 | enoyl-CoA hydratase/carnithine racemase  | 2.766  | 0.108  |
| DespoDRAFT_01933 | N-acetylmuramoyl-L-alanine amidase   | 1.692  | 0.17   |
| DespoDRAFT_01934 | DNA mismatch repair protein MutS   | 1.11   | 0.0162 |
| DespoDRAFT_01935 | hypothetical protein   | 1.265  | 0.512  |
| DespoDRAFT_01936 | putative phosphoesterase ICC   | 1.532  | 0.364  |
| DespoDRAFT_01937 | imidazolonepropionase  | -1.025 | 0.963  |
| DespoDRAFT_01938 | histidine ammonia-lyase  | 1.036  | 0.934  |
| DespoDRAFT_01939 | formyltetrahydrofolate deformylase   | 1.959  | 0.0708 |
| DespoDRAFT_01940 | hypothetical protein   | 1.218  | 0.926  |
| DespoDRAFT_01941 | hypothetical protein   | -1.035 | 0.968  |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_01942 | D-isomer specific 2-hydroxyacid dehydrogenase NAD-binding protein                                | -1.151 | 0.783  |
| DespoDRAFT_01943 | birA biotin-(acetyl-CoA-carboxylase) ligase  | 1.344  | 0.356  |
| DespoDRAFT_01944 | Pyruvate carboxylase   | 1.259  | 0.185  |
| DespoDRAFT_01947 | 2-oxoacid:ferredoxin oxidoreductase gamma subunit  | -2.309 | 0.0859 |
| DespoDRAFT_01948 | Zn-dependent hydrolase glyoxylase  | -1.368 | 0.294  |
| DespoDRAFT_01949 | hypothetical protein   | -1.584 | 0.41   |
| DespoDRAFT_01950 | hypothetical protein   | 1.286  | 0.383  |
| DespoDRAFT_01951 | carbonic anhydrase   | 2.817  | 0.0466 |
| DespoDRAFT_01952 | ATP-dependent exoDNAse (exonuclease V) alpha subunit/helicase superfamily I member               | 1.365  | 0.48   |
| DespoDRAFT_01953 | bacterial nucleoid DNA-binding protein   | 2.537  | 0.199  |
| DespoDRAFT_01954 | methyl-accepting chemotaxis protein  | -2.417 | 0.0543 |
| DespoDRAFT_01955 | anti-anti-sigma regulatory factor (antagonist of anti-sigma factor)                              | -3.074 | 0.156  |
| DespoDRAFT_01956 | response regulator with CheY-like receiver domain and winged-helix DNA-binding domain            | -2.451 | 0.238  |
| DespoDRAFT_01957 | chemotaxis protein histidine kinase-like protein   | -2.007 | 0.26   |
| DespoDRAFT_01958 | chemotaxis signal transduction protein   | -2.503 | 0.157  |
| DespoDRAFT_01959 | methylase of chemotaxis methyl-accepting protein   | -3.289 | 0.0895 |
| DespoDRAFT_01960 | chemotaxis response regulator containing a CheY-like receiver domain and a methylesterase domain | -2.25  | 0.0639 |
| DespoDRAFT_01961 | chemotaxis protein   | -3.102 | 0.0291 |
| DespoDRAFT_01962 | signal transduction histidine kinase   | -1.245 | 0.776  |
| DespoDRAFT_01963 | hypothetical protein   | -4.257 | 0.0842 |
| DespoDRAFT_01964 | outer membrane receptor for ferrienterochelin and colicins                                       | 1.148  | 0.546  |
| DespoDRAFT_01965 | uncharacterized Fe-S center protein  | -2.021 | 0.113  |
| DespoDRAFT_01966 | signal transduction histidine kinase   | -1.744 | 0.221  |
| DespoDRAFT_01967 | hypothetical protein   | 1.383  | 0.185  |
| DespoDRAFT_01968 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains               | -1.438 | 0.498  |
| DespoDRAFT_01969 | hypothetical protein   | -1.325 | 0.35   |
| DespoDRAFT_01970 | hypothetical protein   | 1.973  | 0.434  |
| DespoDRAFT_01971 | AICAR transformylase/IMP cyclohydrolase PurH   | 2.437  | 0.0638 |
| DespoDRAFT_01972 | AICAR transformylase/IMP cyclohydrolase PurH   | 1.619  | 0.104  |

|                  |   |        |        |
|------------------|---|--------|--------|
| DespoDRAFT_01974 | putative transcriptional regulator  | 1.32   | 0.663  |
| DespoDRAFT_01975 | small redox-active disulfide protein 2  | 1.252  | 0.452  |
| DespoDRAFT_01976 | putative permease   | -1.108 | 0.501  |
| DespoDRAFT_01978 | cyclic nucleotide-binding protein   | -1.479 | 0.43   |
| DespoDRAFT_01979 | Rhodanese-related sulfurtransferase   | 1.486  | 0.118  |
| DespoDRAFT_01980 | cation diffusion facilitator family transporter                                       | -1.082 | 0.761  |
| DespoDRAFT_01981 | Rhodanese-related sulfurtransferase   | -1.009 | 0.977  |
| DespoDRAFT_01982 | putative permease   | -1.086 | 0.896  |
| DespoDRAFT_01984 | hypothetical protein  | -1.859 | 0.0242 |
| DespoDRAFT_01988 | PEP-CTERM putative exosortase interaction domain-containing protein                   | -2.258 | 0.112  |
| DespoDRAFT_01989 | exoribonuclease R   | 1.216  | 0.605  |
| DespoDRAFT_01990 | hypothetical protein  | -2.205 | 0.155  |
| DespoDRAFT_01991 | hypothetical protein  | 1.004  | 0.999  |
| DespoDRAFT_01992 | electron transporter RnfB   | 2.788  | 0.0806 |
| DespoDRAFT_01993 | Rnf A subunit   | 2.923  | 0.0696 |
| DespoDRAFT_01994 | Rnf E subunit   | 2.122  | 0.0828 |
| DespoDRAFT_01995 | electron transport complex RnfABCDGE type G subunit                                   | 2.587  | 0.0014 |
| DespoDRAFT_01996 | NADH:ubiquinone oxidoreductase subunit RnfD   | 2.603  | 0.0247 |
| DespoDRAFT_01997 | NADH:ubiquinone oxidoreductase subunit RnfC   | 3.011  | 0.0361 |
| DespoDRAFT_01998 | class III cytochrome C family protein   | 2.569  | 0.0592 |
| DespoDRAFT_01999 | Positive regulator of sigma E activity  | -1.077 | 0.93   |
| DespoDRAFT_02000 | hypothetical protein  | -1.99  | 0.111  |
| DespoDRAFT_02002 | hypothetical protein  | -8.471 | 0.0462 |
| DespoDRAFT_02003 | histidine kinase  | -1.581 | 0.0951 |
| DespoDRAFT_02004 | response regulator with CheY-like receiver domain and winged-helix DNA-binding domain | -1.413 | 0.0682 |
| DespoDRAFT_02005 | hypothetical protein  | 1.071  | 0.673  |
| DespoDRAFT_02006 | Fe-S oxidoreductase   | 1.136  | 0.0731 |
| DespoDRAFT_02007 | nitroreductase  | -1.007 | 0.96   |
| DespoDRAFT_02008 | non-canonical purine NTP pyrophosphatase rdgB/HAM1 family                             | -1.168 | 0.149  |
| DespoDRAFT_02009 | RNA methyltransferase TrmH family group 1   | 4.356  | 0.187  |
| DespoDRAFT_02010 | hypothetical protein  | -1.915 | 0.261  |
| DespoDRAFT_02011 | hypothetical protein  | -2.002 | 0.194  |
| DespoDRAFT_02012 | putative nucleoside-diphosphate sugar epimerase                                       | -1.655 | 0.147  |
| DespoDRAFT_02013 | flavoprotein (flavodoxin)   | 1.307  | 0.319  |
| DespoDRAFT_02014 | Rnf C subunit   | 1.641  | 0.0808 |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_02015 | Rnf D subunit  | 1.967  | 0.0992 |
| DespoDRAFT_02016 | Rnf G subunit  | 1.608  | 0.292  |
| DespoDRAFT_02017 | Rnf E subunit  | 1.148  | 0.42   |
| DespoDRAFT_02018 | Rnf A subunit  | 4.14   | 0.201  |
| DespoDRAFT_02019 | Rnf B subunit  | 2.326  | 0.108  |
| DespoDRAFT_02020 | TIGR00730 family protein   | 1.128  | 0.631  |
| DespoDRAFT_02021 | Flp pilus assembly protein TadD  | 1.192  | 0.225  |
| DespoDRAFT_02022 | PEP-CTERM putative exosortase interaction domain-containing protein          | -2.618 | 0.0262 |
| DespoDRAFT_02023 | Xaa-Pro aminopeptidase   | -2.28  | 0.0338 |
| DespoDRAFT_02024 | lactoylglutathione lyase-like lyase  | -1.892 | 0.307  |
| DespoDRAFT_02025 | hypothetical protein   | -2.936 | 0.0509 |
| DespoDRAFT_02026 | polyferredoxin   | -2.348 | 0.0773 |
| DespoDRAFT_02027 | hypothetical protein   | -4.157 | 0.283  |
| DespoDRAFT_02028 | histidine kinase Response regulator receiver domain protein histidine kinase | -1.412 | 0.251  |
| DespoDRAFT_02029 | ABC-type uncharacterized transport system periplasmic component              | -1.545 | 0.225  |
| DespoDRAFT_02030 | hypothetical protein   | -1.057 | 0.738  |
| DespoDRAFT_02031 | uncharacterized protein involved in formate dehydrogenase formation          | -1.19  | 0.282  |
| DespoDRAFT_02032 | integral membrane protein MviN   | 1.305  | 0.746  |
| DespoDRAFT_02033 | hypothetical protein   | -1.62  | 0.521  |
| DespoDRAFT_02034 | universal stress protein UspA-like protein                                   | -1.111 | 0.661  |
| DespoDRAFT_02035 | methylase involved in ubiquinone/menaquinone biosynthesis                    | -1.532 | 0.156  |
| DespoDRAFT_02036 | mannose-1-phosphate guanylyltransferase/mannose-6-phosphate isomerase        | -1.179 | 0.307  |
| DespoDRAFT_02037 | putative transcriptional regulator   | -1.008 | 0.931  |
| DespoDRAFT_02038 | dynamain family protein  | 1.449  | 0.365  |
| DespoDRAFT_02039 | hypothetical protein   | -1.077 | 0.873  |
| DespoDRAFT_02040 | putative membrane protein  | -1.073 | 0.881  |
| DespoDRAFT_02041 | Dicarboxylate transport  | -1.577 | 0.581  |
| DespoDRAFT_02042 | hypothetical protein   | 1.077  | 0.929  |
| DespoDRAFT_02043 | hypothetical protein   | -1.014 | 0.955  |
| DespoDRAFT_02044 | hypothetical protein   | 1.574  | 0.123  |
| DespoDRAFT_02045 | hypothetical protein   | -2.076 | 0.057  |
| DespoDRAFT_02048 | negative regulator of beta-lactamase expression                              | 1.351  | 0.467  |
| DespoDRAFT_02049 | DNA segregation ATPase FtsK/SpoIIIE family                                   | -1.293 | 0.411  |
| DespoDRAFT_02050 | Protein of unknown function (DUF3108)  | -1.034 | 0.448  |
| DespoDRAFT_02051 | Sua5/YciO/YrdC/Yw1C family protein   | -2.523 | 0.412  |

|                  |   |         |        |
|------------------|---|---------|--------|
| DespoDRAFT_02052 | phosphoribosylamine--glycine ligase/phosphoribosylaminoimidazole carboxylase PurE protein | 1.043   | 0.664  |
| DespoDRAFT_02053 | D-alanine--D-alanine ligase   | 1.082   | 0.0583 |
| DespoDRAFT_02054 | hypothetical protein  | 1.554   | 0.176  |
| DespoDRAFT_02055 | translation elongation factor EF-G  | 1.799   | 0.0674 |
| DespoDRAFT_02056 | putative Zn-dependent protease  | 1.101   | 0.752  |
| DespoDRAFT_02057 | putative inhibitor of MCP methylation CheC  | 2.115   | 0.359  |
| DespoDRAFT_02058 | putative ABC-type transport system permease component                                     | -1.414  | 0.613  |
| DespoDRAFT_02060 | hypothetical protein  | 1.25    | 0.534  |
| DespoDRAFT_02061 | ABC-type proline/glycine betaine transport system periplasmic component                   | -15.818 | 0.0291 |
| DespoDRAFT_02062 | ABC-type proline/glycine betaine transport system permease component                      | -11.172 | 0.0829 |
| DespoDRAFT_02063 | glycine betaine/L-proline transport ATP binding subunit                                   | -9.18   | 0.0465 |
| DespoDRAFT_02064 | cyclic nucleotide-binding protein   | 1.207   | 0.461  |
| DespoDRAFT_02065 | hypothetical protein  | 2.611   | 0.107  |
| DespoDRAFT_02066 | sodium ion-translocating decarboxylase beta subunit                                       | 1.217   | 0.45   |
| DespoDRAFT_02067 | selT/selW/selH selenoprotein domain protein   | 1.306   | 0.671  |
| DespoDRAFT_02068 | signal transduction histidine kinase regulating C4-dicarboxylate transport system         | 1.569   | 0.425  |
| DespoDRAFT_02069 | Cytochrome c bacterial  | -1.647  | 0.0381 |
| DespoDRAFT_02070 | putative thiosulfate reductase  | -1.102  | 0.531  |
| DespoDRAFT_02071 | carboxynorspermidine decarboxylase  | 5.711   | 0.119  |
| DespoDRAFT_02072 | saccharopine dehydrogenase-like oxidoreductase  | 4.021   | 0.1    |
| DespoDRAFT_02073 | succinyl-CoA:acetate CoA transferase  | 2.926   | 0.0241 |
| DespoDRAFT_02075 | hypothetical protein  | 2.527   | 0.27   |
| DespoDRAFT_02076 | NAD(P)H-nitrite reductase   | 2.358   | 0.0842 |
| DespoDRAFT_02077 | protein of unknown function (DUF309)  | -1.529  | 0.475  |
| DespoDRAFT_02080 | hypothetical protein  | 2.002   | NaN    |
| DespoDRAFT_02081 | Transposase IS66 family   | 2.209   | 0.422  |
| DespoDRAFT_02082 | Transposase IS66 family   | -1.739  | 0.29   |
| DespoDRAFT_02083 | class III cytochrome C family protein   | -2.993  | 0.146  |
| DespoDRAFT_02084 | thymidylate kinase  | -1.916  | 0.0619 |
| DespoDRAFT_02086 | putative RNA-binding protein  | -2.66   | 0.125  |
| DespoDRAFT_02087 | NfnA, the alpha subunit of NADH-dependent ferredoxin:NADP oxidoreductase                  | -1.311  | 0.345  |
| DespoDRAFT_02088 | NfnB, the beta subunit of NADH-dependent ferredoxin:NADP oxidoreductase                   | -1.48   | 0.0861 |

|                  |   |          |         |
|------------------|---|----------|---------|
| DespoDRAFT_02089 | Rhodanese-related sulfurtransferase   | -1.005   | 0.993   |
| DespoDRAFT_02090 | phosphoenolpyruvate carboxykinase (GTP)   | -1.044   | 0.33    |
| DespoDRAFT_02091 | putative metal-dependent phosphoesterase<br>PHP family  | -1.013   | 0.929   |
| DespoDRAFT_02092 | hypothetical protein  | -3.563   | NaN     |
| DespoDRAFT_02093 | hypothetical protein  | -1.227   | 0.311   |
| DespoDRAFT_02094 | copper/silver-translocating P-type ATPase<br>heavy metal-translocating P-type ATPase<br>Cd/Co/Hg/Pb/Zn-transporting | -2.036   | 0.0197  |
| DespoDRAFT_02095 | copper chaperone  | -4.692   | 0.061   |
| DespoDRAFT_02096 | cytochrome c biogenesis protein   | 1.115    | 0.747   |
| DespoDRAFT_02097 | Dinitrogenase reductase ADP-<br>ribosyltransferase (DRAT)   | -2.625   | 0.0807  |
| DespoDRAFT_02098 | ADP-ribosyl-(dinitrogen reductase)<br>hydrolase   | -2.446   | 0.0767  |
| DespoDRAFT_02099 | 2-keto-4-pentenoate hydratase/2-oxohepta-<br>3-ene-1,7-dioic acid hydratase   | -1.421   | 0.256   |
| DespoDRAFT_02100 | hypothetical protein  | -4.187   | 0.0659  |
| DespoDRAFT_02106 | hypothetical protein  | -3.034   | 0.0363  |
| DespoDRAFT_02107 | glycosyl transferase  | -2.631   | 0.471   |
| DespoDRAFT_02108 | Protein of unknown function (DUF3047)   | -1.853   | 0.498   |
| DespoDRAFT_02109 | hypothetical protein  | -2.366   | 0.291   |
| DespoDRAFT_02110 | pyruvate/2-oxoglutarate dehydrogenase<br>complex dihydrolipoamide dehydrogenase<br>component                        | -5.399   | 0.0647  |
| DespoDRAFT_02111 | glycosidase   | -3.315   | 0.0883  |
| DespoDRAFT_02112 | hypothetical protein  | -2.088   | 0.151   |
| DespoDRAFT_02113 | hypothetical protein  | -1.178   | 0.795   |
| DespoDRAFT_02114 | beta-ketoacyl synthase  | 2.158    | 0.0355  |
| DespoDRAFT_02115 | 3-oxoacyl-(acyl-carrier-protein) synthase III   | -1.464   | 0.136   |
| DespoDRAFT_02116 | probable alpha/beta hydrolase (EC:3.4.11.5)   | 2.036    | 0.423   |
| DespoDRAFT_02117 | hypothetical protein  | -1.547   | 0.263   |
| DespoDRAFT_02118 | acyl-CoA synthetase (AMP-forming)/AMP-<br>acid ligase II  | -1.198   | 0.624   |
| DespoDRAFT_02119 | hypothetical protein  | -2.132   | 0.0974  |
| DespoDRAFT_02120 | hypothetical protein  | -102.868 | 0.0476  |
| DespoDRAFT_02121 | Fe-S oxidoreductase   | 2.519    | 0.57    |
| DespoDRAFT_02122 | sugar phosphate permease  | 2.892    | 0.177   |
| DespoDRAFT_02123 | ribulose-phosphate 3-epimerase  | 2.237    | 0.298   |
| DespoDRAFT_02124 | ribosomal RNA small subunit<br>methyltransferase RsmB   | 2.962    | 0.119   |
| DespoDRAFT_02125 | methionyl-tRNA formyltransferase  | 2.491    | 0.0705  |
| DespoDRAFT_02126 | peptide deformylase   | 1.593    | 0.224   |
| DespoDRAFT_02127 | riboflavin kinase/FMN adenylyltransferase   | 2.974    | 0.00985 |
| DespoDRAFT_02129 | MiaB-like tRNA modifying enzyme   | -1       | 0.999   |

|                  |  |        |         |
|------------------|--|--------|---------|
| DespoDRAFT_02130 | tRNA (5-methylaminomethyl-2-thiouridylate)-methyltransferase                         | 1.286  | 0.314   |
| DespoDRAFT_02131 | putative ferredoxin  | 1.657  | 0.0354  |
| DespoDRAFT_02132 | PAS domain S-box   | -1.209 | 0.236   |
| DespoDRAFT_02134 | hypothetical protein   | -1.892 | 0.133   |
| DespoDRAFT_02135 | hypothetical protein   | -1.465 | 0.432   |
| DespoDRAFT_02136 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains   | -1.267 | 0.651   |
| DespoDRAFT_02137 | hypothetical protein   | -1.811 | 0.17    |
| DespoDRAFT_02139 | Pyruvate phosphate dikinase  | 1.433  | 0.105   |
| DespoDRAFT_02140 | ATPase component of ABC transporters with duplicated ATPase domain                   | 2.007  | 0.0129  |
| DespoDRAFT_02141 | hypothetical protein   | -1.249 | 0.315   |
| DespoDRAFT_02142 | type IV-A pilus assembly ATPase PilB   | -1.541 | 0.124   |
| DespoDRAFT_02143 | cytochrome c biogenesis factor   | -1.002 | 0.963   |
| DespoDRAFT_02144 | diguanylate cyclase (GGDEF) domain/uncharacterized domain HDIG-containing protein    | -2.237 | 0.038   |
| DespoDRAFT_02145 | hypothetical protein   | -1.669 | 0.307   |
| DespoDRAFT_02146 | nitrogen regulatory protein PII  | -2.119 | 0.103   |
| DespoDRAFT_02147 | ammonium transporter   | 1.127  | 0.428   |
| DespoDRAFT_02148 | hypothetical protein   | -1.139 | 0.918   |
| DespoDRAFT_02149 | PAS domain S-box   | -1.237 | 0.35    |
| DespoDRAFT_02151 | uncharacterized Fe-S center protein  | 1.152  | 0.282   |
| DespoDRAFT_02152 | ATP-binding cassette protein ChvD family   | -1.014 | 0.32    |
| DespoDRAFT_02153 | superfamily II RNA helicase  | 1.265  | 0.261   |
| DespoDRAFT_02154 | 1, 4-dihydroxy-2-naphthoate octaprenyltransferase                                    | 1.216  | 0.699   |
| DespoDRAFT_02155 | adenosine deaminase  | -4.672 | 0.104   |
| DespoDRAFT_02156 | response regulator with CheY-like receiver, AAA-type ATPase, and DNA-binding domains | 1.029  | 0.959   |
| DespoDRAFT_02157 | hypothetical protein   | -1.184 | 0.732   |
| DespoDRAFT_02158 | pyridoxal phosphate enzyme YggS family   | 1.492  | 0.216   |
| DespoDRAFT_02159 | MAF protein  | 1.115  | 0.698   |
| DespoDRAFT_02160 | RNA methyltransferase RsmE family  | -1.191 | 0.217   |
| DespoDRAFT_02162 | Na <sup>+</sup> /H <sup>+</sup> antiporter   | 5.027  | 0.00851 |
| DespoDRAFT_02163 | monovalent cation/proton antiporter MnhG/PhaG subunit                                | -3.077 | 0.36    |
| DespoDRAFT_02164 | multisubunit Na <sup>+</sup> /H <sup>+</sup> antiporter MnhF subunit                 | -1.535 | 0.696   |
| DespoDRAFT_02165 | multisubunit Na <sup>+</sup> /H <sup>+</sup> antiporter MnhE subunit                 | -1.469 | 0.593   |



|                  |   |        |        |
|------------------|---|--------|--------|
| DespoDRAFT_02166 | formate hydrogenlyase subunit<br>3/multisubunit Na <sup>+</sup> /H <sup>+</sup> antiporter MnhD<br>subunit                    | -1.542 | 0.476  |
| DespoDRAFT_02167 | multisubunit Na <sup>+</sup> /H <sup>+</sup> antiporter MnhC<br>subunit   | -1.151 | 0.723  |
| DespoDRAFT_02168 | multisubunit Na <sup>+</sup> /H <sup>+</sup> antiporter MnhB<br>subunit   | -1.171 | NaN    |
| DespoDRAFT_02169 | NADH:ubiquinone oxidoreductase subunit<br>5 (chain L)/multisubunit Na <sup>+</sup> /H <sup>+</sup> antiporter<br>MnhA subunit | -2.712 | 0.0407 |
| DespoDRAFT_02170 | putative membrane protein   | -2.847 | 0.0572 |
| DespoDRAFT_02171 | universal stress protein UspA-like protein  | -1.932 | 0.0365 |
| DespoDRAFT_02172 | glycoside/pentoside/hexuronide transporter  | -1.904 | 0.0949 |
| DespoDRAFT_02173 | hypothetical protein  | -1.304 | 0.185  |
| DespoDRAFT_02174 | hypothetical protein  | -2.034 | 0.0912 |
| DespoDRAFT_02175 | Na <sup>+</sup> /H <sup>+</sup> antiporter NhaD-like permease   | -1.644 | 0.61   |
| DespoDRAFT_02176 | diaminopimelate decarboxylase   | 1.334  | 0.426  |
| DespoDRAFT_02177 | Na <sup>+</sup> /phosphate symporter  | 1.175  | 0.154  |
| DespoDRAFT_02178 | hypothetical protein  | -1.101 | 0.929  |
| DespoDRAFT_02179 | hypothetical protein  | 1.544  | 0.0213 |
| DespoDRAFT_02180 | translation elongation factor EF-G  | 1.481  | 0.235  |
| DespoDRAFT_02181 | 16S rRNA (guanine(527)-N(7))-<br>methyltransferase GidB   | 2.763  | 0.367  |
| DespoDRAFT_02182 | isoleucyl-tRNA synthetase   | 2.355  | 0.0742 |
| DespoDRAFT_02183 | lipoprotein signal peptidase  | 1.092  | 0.929  |
| DespoDRAFT_02184 | prolipoprotein diacylglycerol transferase   | 2.571  | 0.294  |
| DespoDRAFT_02185 | DNA polymerase III delta subunit  | 1.62   | 0.0734 |
| DespoDRAFT_02186 | Pyruvate kinase   | 2.295  | 0.0705 |
| DespoDRAFT_02187 | putative domain HDIG-containing protein   | -1.124 | 0.352  |
| DespoDRAFT_02188 | PAS domain S-box/diguanylate cyclase<br>(GGDEF) domain-containing protein   | -1.741 | 0.235  |
| DespoDRAFT_02189 | ABC-type phosphate transport system<br>periplasmic component  | -1.4   | 0.162  |
| DespoDRAFT_02190 | cyclic nucleotide-binding protein   | -1.067 | 0.79   |
| DespoDRAFT_02191 | hypothetical protein  | 1.675  | 0.33   |
| DespoDRAFT_02192 | RNA methyltransferase RsmE family   | 1.03   | 0.941  |
| DespoDRAFT_02193 | FAD/FMN-dependent dehydrogenase   | -1.317 | 0.466  |
| DespoDRAFT_02194 | peptide chain release factor 3  | 1.978  | 0.0805 |
| DespoDRAFT_02197 | hypothetical protein  | -1.397 | 0.262  |
| DespoDRAFT_02204 | HIT family hydrolase diadenosine<br>tetraphosphate hydrolase  | -2.149 | 0.158  |
| DespoDRAFT_02205 | NAD-dependent protein deacetylase SIR2<br>family  | -2.212 | 0.244  |
| DespoDRAFT_02206 | hypothetical protein  | -1.813 | 0.16   |
| DespoDRAFT_02207 | putative membrane protein   | -1.443 | 0.179  |

|                  |  |         |        |
|------------------|--|---------|--------|
| DespoDRAFT_02208 | glycine cleavage system protein P  | -1.983  | 0.134  |
| DespoDRAFT_02209 | glycine cleavage system protein P  | -1.754  | 0.0451 |
| DespoDRAFT_02210 | glycine cleavage system H protein  | -1.861  | 0.142  |
| DespoDRAFT_02211 | glycine cleavage system T protein<br>(aminomethyltransferase)                            | -2.128  | 0.0573 |
| DespoDRAFT_02212 | transcriptional regulator  | -1.857  | 0.221  |
| DespoDRAFT_02213 | response regulator with CheY-like receiver<br>AAA-type ATPase and DNA-binding<br>domains | -4.631  | 0.0213 |
| DespoDRAFT_02214 | response regulator with CheY-like receiver<br>AAA-type ATPase and DNA-binding<br>domains | -8.851  | 0.0149 |
| DespoDRAFT_02215 | 3-oxoacyl-(acyl-carrier-protein) synthase III  | 2.383   | 0.0805 |
| DespoDRAFT_02216 | glucose-6-phosphate isomerase  | -1.386  | 0.536  |
| DespoDRAFT_02217 | hypothetical protein   | 1.092   | 0.651  |
| DespoDRAFT_02218 | phosphoglucosamine mutase  | -1.163  | 0.188  |
| DespoDRAFT_02219 | ABC-type uncharacterized transport system<br>permease component                          | 1.021   | 0.909  |
| DespoDRAFT_02220 | FtsH-interacting integral membrane protein   | -1.39   | 0.0601 |
| DespoDRAFT_02221 | hypothetical protein   | -1.541  | 0.677  |
| DespoDRAFT_02222 | hypothetical protein   | 1.207   | NaN    |
| DespoDRAFT_02223 | hypothetical protein   | -1.877  | NaN    |
| DespoDRAFT_02224 | phage regulatory protein rha family  | -1.115  | 0.91   |
| DespoDRAFT_02225 | CobQ/CobB/MinD/ParA nucleotide binding<br>domain-containing protein                      | -1.691  | 0.24   |
| DespoDRAFT_02227 | type IV secretory pathway VirB2<br>component (pilin)                                     | -2.93   | 0.486  |
| DespoDRAFT_02228 | Type IV secretory pathway VirB3-like<br>protein  | #VALUE! | NaN    |
| DespoDRAFT_02231 | putative nucleotidyltransferase  | -2.584  | 0.419  |
| DespoDRAFT_02235 | nucleotidyltransferase substrate binding<br>protein HI0074 family                        | 1.366   | 0.69   |
| DespoDRAFT_02236 | hypothetical protein   | #VALUE! | NaN    |
| DespoDRAFT_02237 | hypothetical protein   | -1.476  | 0.131  |
| DespoDRAFT_02238 | CBS domain-containing protein  | -1.243  | 0.227  |
| DespoDRAFT_02240 | putative hydrolase or acyltransferase of<br>alpha/beta superfamily                       | -1.22   | 0.52   |
| DespoDRAFT_02241 | ADP-ribose pyrophosphatase   | -1.636  | 0.412  |
| DespoDRAFT_02242 | NAD-dependent protein deacetylase SIR2<br>family   | -2.29   | 0.119  |
| DespoDRAFT_02243 | 23S rRNA m2A2503 methyltransferase   | -2.509  | 0.21   |
| DespoDRAFT_02244 | membrane protein TerC possibly involved<br>in tellurium resistance                       | 2.795   | 0.128  |
| DespoDRAFT_02245 | D-alanyl-D-alanine carboxypeptidase  | -1.089  | 0.847  |
| DespoDRAFT_02246 | Fe-S oxidoreductase  | 1.287   | 0.321  |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_02247 | transketolase  | 1.493  | 0.0759 |
| DespoDRAFT_02248 | secondary thiamine-phosphate synthase enzyme   | 1.019  | 0.964  |
| DespoDRAFT_02249 | cytochrome c biogenesis factor   | -1.398 | 0.177  |
| DespoDRAFT_02250 | hypothetical protein   | 1.169  | 0.557  |
| DespoDRAFT_02251 | tetratricopeptide repeat protein   | -1.495 | 0.228  |
| DespoDRAFT_02252 | hypothetical protein   | -1.14  | 0.836  |
| DespoDRAFT_02253 | hypothetical protein   | -1.09  | 0.835  |
| DespoDRAFT_02254 | hypothetical protein   | 1.539  | 0.291  |
| DespoDRAFT_02255 | ABC-type multidrug transport system ATPase component   | 3.365  | 0.0857 |
| DespoDRAFT_02256 | ABC transporter  | 2.092  | 0.0497 |
| DespoDRAFT_02257 | ABC-type uncharacterized transporter   | 1.431  | 0.0829 |
| DespoDRAFT_02258 | hypothetical protein   | 1.351  | 0.0168 |
| DespoDRAFT_02259 | 1-acyl-sn-glycerol-3-phosphate acyltransferase   | 1.075  | 0.725  |
| DespoDRAFT_02260 | mraZ protein   | -1.122 | 0.331  |
| DespoDRAFT_02261 | S-adenosyl-methyltransferase MraW  | -1.64  | 0.0945 |
| DespoDRAFT_02262 | Cell division protein FtsL   | -1.451 | 0.133  |
| DespoDRAFT_02263 | cell division protein FtsI/penicillin-binding protein 2  | -1.85  | 0.0409 |
| DespoDRAFT_02264 | UDP-N-acetylmuramyl-tripeptide synthetase/UDP-N-acetylmuramoyl-tripeptide--D-alanyl-D-alanine ligase | -1.259 | 0.451  |
| DespoDRAFT_02265 | phospho-N-acetylmuramoyl-pentapeptide-transferase  | -1.539 | 0.224  |
| DespoDRAFT_02266 | UDP-N-acetylmuramoylalanine--D-glutamate ligase  | -1.094 | 0.843  |
| DespoDRAFT_02267 | cell division protein FtsW   | -1.953 | 0.0709 |
| DespoDRAFT_02268 | undecaprenyldiphospho-muramoylpentapeptide beta-N-acetylglucosaminyltransferase                      | 1.026  | 0.911  |
| DespoDRAFT_02269 | UDP-N-acetylmuramate--alanine ligase   | 1.099  | 0.732  |
| DespoDRAFT_02270 | UDP-N-acetylenolpyruvoylglucosamine reductase  | 1.115  | 0.771  |
| DespoDRAFT_02271 | cell division septal protein   | -1.084 | 0.772  |
| DespoDRAFT_02272 | cell division protein FtsA   | 1.438  | 0.0992 |
| DespoDRAFT_02273 | cell division protein FtsZ   | -1.326 | 0.377  |
| DespoDRAFT_02274 | DNA/RNA helicase superfamily II  | 4.325  | 0.0217 |
| DespoDRAFT_02276 | hypothetical protein   | -1.903 | 0.217  |
| DespoDRAFT_02277 | hypothetical protein   | -2.884 | 0.181  |
| DespoDRAFT_02280 | putative nucleoside-diphosphate sugar epimerase  | -2.257 | 0.198  |
| DespoDRAFT_02281 | putative flavin-nucleotide-binding protein   | 1.606  | 0.829  |

|                  |  |        |         |
|------------------|--|--------|---------|
| DespoDRAFT_02282 | histidine kinase, Response regulator receiver domain protein, histidine kinase GAF domain-containing protein | 1.1    | 0.894   |
| DespoDRAFT_02283 | putative NAD/FAD-binding protein   | -2.32  | 0.16    |
| DespoDRAFT_02284 | methyltransferase, cyclopropane fatty acid synthase  | -2.624 | 0.134   |
| DespoDRAFT_02285 | dehydrogenase of unknown specificity   | -6.502 | 0.0123  |
| DespoDRAFT_02286 | hypothetical protein   | -4.719 | 0.00976 |
| DespoDRAFT_02287 | hypothetical protein   | -5.26  | 0.0759  |
| DespoDRAFT_02288 | hypothetical protein   | -1.188 | 0.228   |
| DespoDRAFT_02289 | MIP family channel protein   | -1.058 | 0.538   |
| DespoDRAFT_02291 | hypothetical protein   | -1.585 | 0.156   |
| DespoDRAFT_02292 | hypothetical protein   | -1.88  | 0.219   |
| DespoDRAFT_02294 | hypothetical protein   | 1.044  | 0.944   |
| DespoDRAFT_02298 | methylase involved in ubiquinone/menaquinone biosynthesis  | 1.092  | 0.835   |
| DespoDRAFT_02299 | CBS domain-containing protein  | 1.212  | 0.771   |
| DespoDRAFT_02300 | lipid-A-disaccharide synthase  | 3.124  | 0.172   |
| DespoDRAFT_02301 | hypothetical protein   | 1.781  | 0.188   |
| DespoDRAFT_02302 | acyl-(acyl-carrier-protein)--UDP-N-acetylglucosamine O-acyltransferase                                       | 2.198  | 0.205   |
| DespoDRAFT_02303 | UDP-3-O-(3-hydroxymyristoyl) glucosamine N-acyltransferase   | 1.028  | 0.914   |
| DespoDRAFT_02304 | outer membrane protein   | 2.049  | 0.116   |
| DespoDRAFT_02305 | outer membrane protein assembly complex YaeT protein   | 1.545  | 0.38    |
| DespoDRAFT_02306 | ABC-type antimicrobial peptide transport system ATPase component   | 1.719  | 0.315   |
| DespoDRAFT_02307 | lipoprotein releasing system transmembrane protein LolC/E family   | 2.194  | 0.245   |
| DespoDRAFT_02308 | lysyl-tRNA synthetase (class II)   | 2.165  | 0.059   |
| DespoDRAFT_02309 | heterodisulfide reductase subunit B  | 3.988  | 0.173   |
| DespoDRAFT_02310 | Nitrate reductase gamma subunit  | 5.035  | 0.0634  |
| DespoDRAFT_02311 | signal transduction histidine kinase nitrogen specific   | -1.027 | 0.96    |
| DespoDRAFT_02312 | type II secretory pathway component PulF   | -1.665 | 0.311   |
| DespoDRAFT_02313 | tRNA nucleotidyltransferase/poly(A) polymerase   | -1.821 | 0.298   |
| DespoDRAFT_02314 | tryptophanyl-tRNA synthetase   | 2.633  | 0.0777  |
| DespoDRAFT_02315 | pseudouridine synthase family protein  | -1.131 | 0.466   |
| DespoDRAFT_02316 | glutamate N-acetyltransferase/amino-acid acetyltransferase   | 1.166  | 0.326   |
| DespoDRAFT_02317 | transcriptional regulator  | -1.738 | 0.202   |
| DespoDRAFT_02318 | Sulfate permease-like transporter MFS superfamily (Sulp3), high affinity sulfate                             | -2.94  | 0.0209  |

|                  |  |        |        |
|------------------|--|--------|--------|
|                  | transporter.   |        |        |
| DespoDRAFT_02319 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains | -2.154 | 0.0353 |
| DespoDRAFT_02320 | histidine kinase   | -2.581 | 0.0679 |
| DespoDRAFT_02321 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains | -1.837 | 0.236  |
| DespoDRAFT_02322 | hypothetical protein   | -1.292 | 0.283  |
| DespoDRAFT_02323 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains | -2.472 | 0.0786 |
| DespoDRAFT_02328 | hypothetical protein   | 1.782  | 0.387  |
| DespoDRAFT_02329 | 3-deoxy-D-manno-octulosonic-acid transferase                                       | 1.019  | 0.973  |
| DespoDRAFT_02330 | ABC-type multidrug transport system ATPase and permease component                  | 2.221  | 0.186  |
| DespoDRAFT_02331 | hypothetical protein   | -1.187 | 0.514  |
| DespoDRAFT_02332 | hypothetical protein   | 1.761  | 0.502  |
| DespoDRAFT_02333 | TIGR00255 family protein   | -1.08  | 0.743  |
| DespoDRAFT_02334 | hypothetical protein   | -1.147 | 0.484  |
| DespoDRAFT_02335 | guanylate kinase   | -1.014 | 0.979  |
| DespoDRAFT_02336 | rRNA methylase putative group 3  | 1.442  | 0.0946 |
| DespoDRAFT_02337 | putative amidophosphoribosyltransferase  | -1.544 | 0.676  |
| DespoDRAFT_02338 | DNA/RNA helicase superfamily II  | 1.543  | 0.261  |
| DespoDRAFT_02339 | hypothetical protein   | 1.34   | 0.707  |
| DespoDRAFT_02340 | abortive infection bacteriophage resistance protein                                | 1.092  | 0.486  |
| DespoDRAFT_02341 | adenine-specific DNA methylase containing a Zn-ribbon                              | 1.633  | 0.311  |
| DespoDRAFT_02342 | putative ATPase (AAA+ superfamily)   | 1.439  | 0.255  |
| DespoDRAFT_02343 | glucosamine 6-phosphate synthetase   | 1.844  | 0.0797 |
| DespoDRAFT_02344 | cell division protein FtsI/penicillin-binding protein 2                            | 3.263  | 0.086  |
| DespoDRAFT_02345 | protein containing C-terminal region/beta chain of methionyl-tRNA synthetase       | 1.373  | 0.108  |
| DespoDRAFT_02346 | putative PSP1-like protein   | -1.033 | 0.864  |
| DespoDRAFT_02347 | DNA polymerase III delta" subunit  | 1.114  | 0.775  |
| DespoDRAFT_02348 | bacterial nucleoid DNA-binding protein   | 1.583  | 0.186  |
| DespoDRAFT_02349 | transcription antiterminator   | 1.467  | 0.734  |
| DespoDRAFT_02350 | organic solvent tolerance protein OstA   | 1.908  | 0.193  |
| DespoDRAFT_02351 | cysteine synthase  | 1.769  | 0.0488 |
| DespoDRAFT_02352 | hypothetical protein   | 2.388  | 0.21   |
| DespoDRAFT_02353 | iron sulfur cluster binding protein (4Fe-4S  | 1.925  | 0.29   |

|                  |  |        |        |
|------------------|--|--------|--------|
|                  | ferredoxin family protein)   |        |        |
| DespoDRAFT_02354 | DMT(drug/metabolite transporter) superfamily permease                      | 2.641  | 0.0945 |
| DespoDRAFT_02357 | DMT(drug/metabolite transporter) superfamily permease                      | 2.182  | NaN    |
| DespoDRAFT_02359 | hypothetical protein   | -1.027 | 0.965  |
| DespoDRAFT_02360 | hypothetical protein   | 1.127  | 0.498  |
| DespoDRAFT_02361 | flagellar motor component  | 1.178  | 0.302  |
| DespoDRAFT_02362 | flagellar motor protein  | -1.759 | 0.177  |
| DespoDRAFT_02363 | hypothetical protein   | -1.631 | 0.728  |
| DespoDRAFT_02364 | PilZ domain-containing protein   | -1.463 | 0.361  |
| DespoDRAFT_02365 | hypothetical protein   | -1.076 | 0.929  |
| DespoDRAFT_02368 | hypothetical protein   | -1.887 | 0.522  |
| DespoDRAFT_02372 | YgiT-type zinc finger domain protein                                       | -1.977 | 0.224  |
| DespoDRAFT_02373 | putative Fe-S oxidoreductase   | -1.096 | 0.497  |
| DespoDRAFT_02374 | recombination protein RecR   | -1.018 | 0.959  |
| DespoDRAFT_02375 | DNA-binding protein YbaB/EbfC family                                       | 1.233  | 0.414  |
| DespoDRAFT_02376 | DNA polymerase III subunit gamma/tau                                       | 1.308  | 0.348  |
| DespoDRAFT_02377 | general secretion pathway protein G  | 1.18   | 0.33   |
| DespoDRAFT_02378 | prepilin-type N-terminal cleavage/methylation domain-containing protein    | 1.256  | 0.257  |
| DespoDRAFT_02379 | prepilin-type N-terminal cleavage/methylation domain-containing protein    | -1     | 0.998  |
| DespoDRAFT_02380 | prepilin-type N-terminal cleavage/methylation domain-containing protein    | -1.241 | 0.494  |
| DespoDRAFT_02381 | type II secretory pathway component PulK                                   | -1.403 | 0.167  |
| DespoDRAFT_02382 | General secretion pathway protein L (GspL)                                 | 1.068  | 0.893  |
| DespoDRAFT_02383 | General secretion pathway M protein  | 2.462  | 0.337  |
| DespoDRAFT_02384 | general secretion pathway protein D  | 1.531  | 0.0734 |
| DespoDRAFT_02385 | general secretory pathway protein E  | 1.705  | 0.341  |
| DespoDRAFT_02386 | hypothetical protein   | 1.004  | 0.98   |
| DespoDRAFT_02387 | hydroxylamine reductase  | -5.076 | 0.0727 |
| DespoDRAFT_02390 | NAD+ synthetase  | 1.568  | 0.176  |
| DespoDRAFT_02391 | rRNA methylase   | 1.819  | 0.59   |
| DespoDRAFT_02392 | hypothetical protein   | 1.361  | 0.427  |
| DespoDRAFT_02393 | fructose-bisphosphate aldolase class II                                    | -1.511 | 0.0359 |
| DespoDRAFT_02394 | ABC-type dipeptide transport system periplasmic component                  | -1.904 | 0.0773 |
| DespoDRAFT_02395 | ABC-type dipeptide/oligopeptide/nickel transport system permease component | -2.081 | 0.19   |
| DespoDRAFT_02396 | ABC-type dipeptide/oligopeptide/nickel                                     | 1.044  | 0.943  |

|                  |  |        |        |
|------------------|--|--------|--------|
|                  | transport system permease component  |        |        |
| DespoDRAFT_02397 | ABC-type dipeptide/oligopeptide/nickel transport system ATPase component           | 1.232  | 0.788  |
| DespoDRAFT_02398 | ABC-type dipeptide/oligopeptide/nickel transport system ATPase component           | -1.045 | 0.891  |
| DespoDRAFT_02399 | SH3 domain-containing protein  | 1.133  | 0.623  |
| DespoDRAFT_02400 | purine nucleoside phosphorylase I  | -1.23  | 0.49   |
| DespoDRAFT_02401 | hypothetical protein   | -1.129 | 0.287  |
| DespoDRAFT_02402 | hypothetical protein   | -1.567 | 0.536  |
| DespoDRAFT_02403 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains | -1.452 | 0.695  |
| DespoDRAFT_02404 | anion transporter  | 1.098  | 0.927  |
| DespoDRAFT_02405 | hypothetical protein   | 1.088  | NaN    |
| DespoDRAFT_02406 | outer membrane protein/peptidoglycan-associated (lipo)protein                      | -1.087 | 0.638  |
| DespoDRAFT_02407 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains | -1.451 | 0.343  |
| DespoDRAFT_02408 | histidine kinase HAMP domain-containing protein histidine kinase                   | -1.51  | 0.138  |
| DespoDRAFT_02409 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains | 1.291  | 0.375  |
| DespoDRAFT_02410 | histidine kinase Response regulator receiver domain protein histidine kinase       | 1.141  | 0.738  |
| DespoDRAFT_02411 | anion transporter  | -1.036 | 0.922  |
| DespoDRAFT_02412 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains | -1.34  | 0.284  |
| DespoDRAFT_02413 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains | -1.054 | 0.922  |
| DespoDRAFT_02414 | histidine kinase   | -1.99  | 0.498  |
| DespoDRAFT_02416 | universal stress protein UspA-like protein   | -5.806 | 0.0788 |
| DespoDRAFT_02417 | universal stress protein UspA-like protein   | -2.528 | 0.0122 |
| DespoDRAFT_02419 | hypothetical protein   | -4.09  | 0.183  |
| DespoDRAFT_02420 | methionine-R-sulfoxide reductase/methionine-S-sulfoxide reductase                  | -3.306 | 0.102  |
| DespoDRAFT_02422 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains | 1.227  | 0.545  |
| DespoDRAFT_02423 | protein-tyrosine-phosphatase   | -1.119 | 0.792  |
| DespoDRAFT_02424 | polyphosphate kinase 1   | -1.871 | 0.101  |
| DespoDRAFT_02425 | ribosome-associated GTPase EngA  | -2.082 | 0.029  |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_02426 | AAA ATPase   | -1.633 | 0.327  |
| DespoDRAFT_02427 | hypothetical protein   | 1.251  | 0.65   |
| DespoDRAFT_02428 | putative permease  | 1.259  | 0.352  |
| DespoDRAFT_02429 | DNA gyrase A subunit   | 1.049  | 0.764  |
| DespoDRAFT_02430 | DNA repair protein radc  | -1.597 | 0.0691 |
| DespoDRAFT_02431 | hypothetical protein   | -1.391 | 0.469  |
| DespoDRAFT_02432 | 3-phosphoglycerate kinase  | -1.167 | 0.429  |
| DespoDRAFT_02433 | hypothetical protein   | -1.431 | 0.145  |
| DespoDRAFT_02434 | acetyltransferase N-acetylglutamate synthase   | -1.848 | 0.165  |
| DespoDRAFT_02436 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains               | -2.106 | 0.33   |
| DespoDRAFT_02437 | methylase of chemotaxis methyl-accepting protein   | -1.829 | 0.364  |
| DespoDRAFT_02438 | chemotaxis response regulator containing a CheY-like receiver domain and a methylesterase domain | -2.875 | 0.177  |
| DespoDRAFT_02439 | chemotaxis signal transduction protein   | -3.166 | 0.0438 |
| DespoDRAFT_02440 | chemotaxis protein histidine kinase-like protein   | -2.902 | 0.0571 |
| DespoDRAFT_02441 | collagenase-like protease  | 1.046  | 0.833  |
| DespoDRAFT_02443 | soluble lytic murein transglycosylase-like protein   | 2.323  | 0.235  |
| DespoDRAFT_02448 | ribosomal protein L33  | -1.435 | 0.157  |
| DespoDRAFT_02450 | preprotein translocase SecE subunit  | -1.03  | 0.921  |
| DespoDRAFT_02451 | transcription termination/antitermination factor NusG  | -1.011 | 0.963  |
| DespoDRAFT_02452 | 50S ribosomal protein L11  | 1.493  | 0.22   |
| DespoDRAFT_02453 | ribosomal protein L1   | 1.345  | 0.116  |
| DespoDRAFT_02454 | ribosomal protein L10  | 2.625  | 0.0337 |
| DespoDRAFT_02455 | ribosomal protein L7/L12   | 2.28   | 0.068  |
| DespoDRAFT_02456 | DNA-directed RNA polymerase beta subunit   | -1.068 | 0.345  |
| DespoDRAFT_02457 | DNA-directed RNA polymerase beta" subunit predominant form                                       | 1.148  | 0.233  |
| DespoDRAFT_02458 | ribosomal protein S12 bacterial/organelle  | 1.414  | 0.193  |
| DespoDRAFT_02459 | ribosomal protein S7 bacterial/organelle   | 2.016  | 0.156  |
| DespoDRAFT_02460 | translation elongation factor TU   | 1.787  | 0.08   |
| DespoDRAFT_02461 | ribosomal protein S10 bacterial/organelle  | 1.947  | 0.0475 |
| DespoDRAFT_02462 | 50S ribosomal protein L3 bacterial   | 1.546  | 0.0587 |
| DespoDRAFT_02463 | 50S ribosomal protein L4 bacterial/organelle   | 1.771  | 0.0521 |
| DespoDRAFT_02464 | ribosomal protein L23  | 1.863  | 0.143  |
| DespoDRAFT_02465 | ribosomal protein L2 bacterial/organelle   | 2.002  | 0.0196 |



|                  |   |        |        |
|------------------|---|--------|--------|
| DespoDRAFT_02466 | ribosomal protein S19 bacterial/organelle             | 2.492  | 0.0756 |
| DespoDRAFT_02467 | ribosomal protein L22 bacterial type                  | 1.866  | 0.127  |
| DespoDRAFT_02468 | ribosomal protein S3 bacterial type                   | 1.832  | 0.0361 |
| DespoDRAFT_02469 | ribosomal protein L16 bacterial/organelle             | 1.703  | 0.101  |
| DespoDRAFT_02470 | ribosomal protein L29                                 | 1.945  | 0.0724 |
| DespoDRAFT_02471 | 30S ribosomal protein S17                             | 1.981  | 0.0472 |
| DespoDRAFT_02472 | ribosomal protein L14 bacterial/organelle             | 2.351  | 0.0072 |
| DespoDRAFT_02473 | ribosomal protein L24 bacterial/organelle             | 2.478  | 0.132  |
| DespoDRAFT_02474 | ribosomal protein L5                                  | 2.145  | 0.0564 |
| DespoDRAFT_02475 | ribosomal protein S14                                 | 2.22   | 0.11   |
| DespoDRAFT_02476 | ribosomal protein S8                                  | 2.599  | 0.0431 |
| DespoDRAFT_02477 | ribosomal protein L6 bacterial type                   | 2.486  | 0.0605 |
| DespoDRAFT_02478 | ribosomal protein L18 bacterial type                  | 2.121  | 0.0498 |
| DespoDRAFT_02479 | ribosomal protein S5 bacterial/organelle type         | 2.505  | 0.0778 |
| DespoDRAFT_02480 | ribosomal protein L30 bacterial/organelle             | 2.45   | 0.1    |
| DespoDRAFT_02481 | ribosomal protein L15 bacterial/organelle             | 1.646  | 0.143  |
| DespoDRAFT_02482 | preprotein translocase SecY subunit                   | 1.573  | 0.0724 |
| DespoDRAFT_02483 | translation initiation factor IF-1                    | 2.009  | 0.0887 |
| DespoDRAFT_02484 | ribosomal protein L36 bacterial type                  | 1.416  | 0.298  |
| DespoDRAFT_02485 | 30S ribosomal protein S13                             | 2.231  | 0.0422 |
| DespoDRAFT_02486 | 30S ribosomal protein S11                             | 2.125  | 0.0466 |
| DespoDRAFT_02487 | ribosomal protein S4 bacterial/organelle type         | 2.566  | 0.0773 |
| DespoDRAFT_02488 | DNA-directed RNA polymerase alpha subunit             | 1.999  | 0.0474 |
| DespoDRAFT_02489 | ribosomal protein L17                                 | 1.439  | 0.214  |
| DespoDRAFT_02490 | hypothetical protein                                  | 1.801  | 0.473  |
| DespoDRAFT_02491 | molybdenum cofactor biosynthesis protein A            | 1.863  | 0.11   |
| DespoDRAFT_02492 | uroporphyrin-III C-methyltransferase                  | 2.161  | 0.0518 |
| DespoDRAFT_02493 | porphobilinogen deaminase                             | 2.571  | 0.0565 |
| DespoDRAFT_02494 | putative regulatory protein FmdB family               | 3.44   | 0.0471 |
| DespoDRAFT_02495 | amidohydrolase  | -1.971 | 0.0439 |
| DespoDRAFT_02496 | hypothetical protein                                  | 1.56   | 0.0989 |
| DespoDRAFT_02497 | phosphoheptose isomerase                              | 1.346  | 0.212  |
| DespoDRAFT_02498 | tetratricopeptide repeat protein                      | -2.453 | 0.119  |
| DespoDRAFT_02499 | seryl-tRNA(Sec) selenium transferase                  | -1.249 | 0.402  |
| DespoDRAFT_02500 | putative domain HDIG-containing protein               | -1.332 | 0.346  |
| DespoDRAFT_02501 | diguanylate cyclase (GGDEF) domain-containing protein | -1.096 | 0.855  |
| DespoDRAFT_02502 | orotidine 5"-phosphate decarboxylase subfamily 1      | 1.206  | 0.224  |
| DespoDRAFT_02503 | aspartate kinase monofunctional class                 | 4.095  | 0.0278 |
| DespoDRAFT_02504 | ATPase YjeE family                                    | 1.187  | 0.814  |

|                  |   |        |        |
|------------------|---|--------|--------|
| DespoDRAFT_02505 | yjeF-like protein   | -1.024 | 0.935  |
| DespoDRAFT_02506 | 3-methyladenine DNA glycosylase   | 1.138  | 0.368  |
| DespoDRAFT_02507 | ABC-type uncharacterized transport system permease and ATPase component | -1.231 | 0.235  |
| DespoDRAFT_02508 | hypothetical protein  | 1.862  | 0.0608 |
| DespoDRAFT_02509 | putative metal-binding protein  | 1.663  | 0.148  |
| DespoDRAFT_02510 | 2-C-methyl-D-erythritol 2 4-cyclodiphosphate synthase                   | 1.371  | 0.134  |
| DespoDRAFT_02511 | cysteinyl-tRNA synthetase   | 1.744  | 0.0862 |
| DespoDRAFT_02512 | glutaminyt-tRNA synthetase  | 1.337  | 0.0894 |
| DespoDRAFT_02513 | putative CoA-binding protein  | 1.875  | 0.382  |
| DespoDRAFT_02514 | excinuclease ABC B subunit  | -1.335 | 0.145  |
| DespoDRAFT_02515 | hypothetical protein  | -1.478 | 0.285  |
| DespoDRAFT_02516 | Protein of unknown function (DUF2442)                                   | -2.461 | 0.128  |
| DespoDRAFT_02518 | PKD domain protein  | 1.3    | 0.644  |
| DespoDRAFT_02520 | Retron-type reverse transcriptase                                       | 3.173  | 0.0301 |
| DespoDRAFT_02522 | cysteine protease   | 1.856  | 0.298  |
| DespoDRAFT_02523 | PEP-CTERM putative exosortase interaction domain-containing protein     | -2.925 | 0.182  |
| DespoDRAFT_02524 | rubredoxin  | -1.412 | 0.537  |
| DespoDRAFT_02525 | putative nucleotidyltransferase   | 1.548  | 0.506  |
| DespoDRAFT_02526 | hypothetical protein  | 1.069  | 0.898  |
| DespoDRAFT_02527 | excinuclease ABC C subunit  | -1.233 | 0.0833 |
| DespoDRAFT_02528 | ribosomal protein S1  | 2.352  | 0.0525 |
| DespoDRAFT_02529 | putative HAD superfamily hydrolase                                      | 1.921  | 0.188  |
| DespoDRAFT_02530 | PAS domain S-box  | 1.117  | 0.824  |
| DespoDRAFT_02531 | pyridoxine 5"-phosphate synthase  | 1.064  | 0.851  |
| DespoDRAFT_02532 | metalloprotein YbeY/UPF0054 family                                      | -1.069 | 0.923  |
| DespoDRAFT_02533 | putative domain HDIG-containing protein                                 | 1.44   | 0.409  |
| DespoDRAFT_02534 | phosphate starvation-inducible protein PhoH predicted ATPase            | 1.95   | 0.219  |
| DespoDRAFT_02535 | putative membrane protein required for colicin V production             | -1.048 | 0.86   |
| DespoDRAFT_02536 | MazG family protein   | -1.138 | 0.33   |
| DespoDRAFT_02537 | hypothetical protein  | -4.125 | 0.0859 |
| DespoDRAFT_02538 | flagellar biosynthesis anti-sigma factor FlgM                           | -1.786 | 0.174  |
| DespoDRAFT_02539 | hypothetical protein  | -1.375 | 0.123  |
| DespoDRAFT_02540 | fructose/tagatose bisphosphate aldolase                                 | -1.543 | 0.157  |
| DespoDRAFT_02541 | transcriptional regulator   | 2.172  | 0.0352 |
| DespoDRAFT_02542 | Fe-S oxidoreductase   | 5.746  | 0.0165 |
| DespoDRAFT_02543 | Electron transfer flavoprotein beta subunit                             | 3.515  | 0.0522 |
| DespoDRAFT_02544 | electron transfer flavoprotein alpha subunit                            | 3.568  | 0.0122 |
| DespoDRAFT_02545 | thymidylate synthase  | -1.15  | 0.653  |
| DespoDRAFT_02546 | putative ATPase (AAA+ superfamily)                                      | 1.013  | 0.829  |

|                  |   |        |       |
|------------------|---|--------|-------|
| DespoDRAFT_02547 | hypothetical protein  | 1.504  | 0.324 |
| DespoDRAFT_02548 | Protein of unknown function (DUF3423)                       | 1.097  | 0.651 |
| DespoDRAFT_02549 | CRISPR-associated endonuclease Cas1                         | -3.398 | 0.685 |
| DespoDRAFT_02550 | hypothetical protein  | 2.239  | NaN   |
| DespoDRAFT_02551 | hypothetical protein  | -2.762 | 0.467 |
| DespoDRAFT_02552 | hypothetical protein  | -1.229 | 0.782 |
| DespoDRAFT_02553 | hypothetical protein  | -2.134 | 0.115 |
| DespoDRAFT_02554 | hypothetical protein  | -1.791 | 0.262 |
| DespoDRAFT_02555 | hypothetical protein  | -1.458 | 0.155 |
| DespoDRAFT_02556 | Protein of unknown function (DUF1703)                       | -1.006 | 0.986 |
| DespoDRAFT_02557 | CRISPR-associated endoribonuclease Cas2                     | 1.062  | 0.801 |
| DespoDRAFT_02558 | CRISPR type III-A/MTUBE-associated RAMP protein Csm5        | 1.545  | 0.401 |
| DespoDRAFT_02559 | hypothetical protein  | 1.413  | 0.544 |
| DespoDRAFT_02560 | CRISPR type III-A/MTUBE-associated RAMP protein Csm3        | 1.342  | 0.307 |
| DespoDRAFT_02561 | CRISPR type III-A/MTUBE-associated protein Csm2             | 2.227  | 0.381 |
| DespoDRAFT_02562 | CRISPR-associated protein Cas10/Csm1 subtype III-A/MTUBE    | 1.142  | 0.489 |
| DespoDRAFT_02563 | CRISPR-associated protein TM1812 family                     | 1.483  | 0.216 |
| DespoDRAFT_02564 | hypothetical protein  | 2.416  | 0.227 |
| DespoDRAFT_02565 | hypothetical protein  | 1.727  | 0.664 |
| DespoDRAFT_02567 | putative CRISPR-associated protein APE2256 family           | -1.138 | 0.649 |
| DespoDRAFT_02568 | CRISPR-associated protein TM1812 family                     | -1.342 | 0.138 |
| DespoDRAFT_02569 | CRISPR type III-B/RAMP module RAMP protein Cmr6             | -1.178 | 0.314 |
| DespoDRAFT_02570 | CRISPR type III-B/RAMP module-associated protein Cmr5       | 1.158  | 0.778 |
| DespoDRAFT_02571 | CRISPR type III-B/RAMP module RAMP protein Cmr4             | -1.31  | 0.664 |
| DespoDRAFT_02572 | CRISPR-associated protein                                   | -1.344 | 0.421 |
| DespoDRAFT_02573 | CRISPR-associated protein Cas10/Cmr2 subtype III-B          | -1.186 | 0.719 |
| DespoDRAFT_02574 | CRISPR type III-B/RAMP module RAMP protein Cmr1             | -1.503 | 0.139 |
| DespoDRAFT_02575 | hypothetical protein  | -2.012 | 0.233 |
| DespoDRAFT_02576 | hypothetical protein  | -1.209 | 0.755 |
| DespoDRAFT_02577 | hypothetical protein  | 1.228  | 0.61  |
| DespoDRAFT_02578 | methylase involved in ubiquinone/menaquinone biosynthesis   | -1.335 | 0.669 |
| DespoDRAFT_02579 | anaerobic dehydrogenase typically selenocysteine-containing | 1.283  | 0.71  |
| DespoDRAFT_02580 | class III cytochrome C family protein                       | 1.495  | 0.162 |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_02581 | twin arginine targeting protein translocase subunit TatC                           | -1.091 | 0.56   |
| DespoDRAFT_02582 | Sec-independent protein secretion pathway component                                | 1.165  | 0.653  |
| DespoDRAFT_02583 | DNA/RNA helicase superfamily II  | 1.443  | 0.154  |
| DespoDRAFT_02584 | putative integral membrane protein   | -1.635 | 0.142  |
| DespoDRAFT_02585 | DivIVA domain protein  | -1.366 | 0.282  |
| DespoDRAFT_02586 | pilus retraction protein PilT  | -1.116 | 0.644  |
| DespoDRAFT_02587 | pilus retraction protein PilT  | -1.561 | 0.116  |
| DespoDRAFT_02588 | hypothetical protein   | -1.289 | 0.313  |
| DespoDRAFT_02589 | hypothetical protein   | -1.334 | 0.583  |
| DespoDRAFT_02590 | penicillin-binding protein, 1A family  | 1.232  | 0.159  |
| DespoDRAFT_02591 | sporulation related protein  | 1.896  | 0.143  |
| DespoDRAFT_02592 | hypothetical protein   | -3.688 | 0.0734 |
| DespoDRAFT_02593 | hypothetical protein   | -3.102 | 0.152  |
| DespoDRAFT_02594 | hypothetical protein   | -1.315 | 0.124  |
| DespoDRAFT_02595 | selenium metabolism protein YedF   | -1.155 | 0.467  |
| DespoDRAFT_02596 | putative Fe-S oxidoreductase   | -1.953 | 0.402  |
| DespoDRAFT_02597 | tRNA-dihydrouridine synthase   | -1.127 | 0.874  |
| DespoDRAFT_02598 | hypothetical protein   | -3.031 | 0.0873 |
| DespoDRAFT_02599 | putative virion core protein (lumpy skin disease virus)                            | -2.026 | 0.0478 |
| DespoDRAFT_02600 | Fe <sup>2+</sup> /Zn <sup>2+</sup> uptake regulation protein                       | 1.498  | 0.145  |
| DespoDRAFT_02601 | hypothetical protein   | 1.99   | 0.18   |
| DespoDRAFT_02603 | hypothetical protein   | 1.773  | 0.183  |
| DespoDRAFT_02604 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains | -1.291 | 0.024  |
| DespoDRAFT_02605 | signal transduction histidine kinase   | -1.246 | 0.0616 |
| DespoDRAFT_02606 | type IV pilus assembly protein PilM  | -3.974 | 0.054  |
| DespoDRAFT_02607 | Tfp pilus assembly protein PilN  | -3.181 | 0.0861 |
| DespoDRAFT_02608 | Tfp pilus assembly protein PilO  | -3.35  | 0.0492 |
| DespoDRAFT_02609 | Tfp pilus assembly protein PilP  | -4.313 | 0.0661 |
| DespoDRAFT_02610 | type IV pilus secretin PilQ/competence protein                                     | -3.294 | 0.067  |
| DespoDRAFT_02611 | Tfp pilus assembly protein PilF  | -2.315 | 0.431  |
| DespoDRAFT_02612 | hypothetical protein   | -1.992 | 0.193  |
| DespoDRAFT_02613 | threonine synthase   | -1.148 | 0.292  |
| DespoDRAFT_02614 | seryl-tRNA synthetase  | -1.011 | 0.936  |
| DespoDRAFT_02615 | 5, 10-methenyltetrahydrofolate synthetase  | 1.33   | 0.377  |
| DespoDRAFT_02616 | K <sup>+</sup> transport system NAD-binding component                              | 1.028  | 0.896  |
| DespoDRAFT_02617 | protein-L-isoaspartate and D-aspartate O-methyltransferase                         | -1.372 | 0.176  |
| DespoDRAFT_02618 | putative membrane protein  | 1.274  | 0.791  |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_02619 | HD-GYP domain-containing protein   | 1.8    | 0.157  |
| DespoDRAFT_02620 | disulfide bond chaperone   | 1.147  | 0.229  |
| DespoDRAFT_02621 | periplasmic component of amino acid ABC-type transporter/signal transduction system    | -2.224 | 0.107  |
| DespoDRAFT_02622 | PAS domain S-box   | -3.076 | 0.0832 |
| DespoDRAFT_02623 | Flavin reductase   | 1.124  | 0.235  |
| DespoDRAFT_02624 | Mg chelatase-related protein   | -1.311 | 0.51   |
| DespoDRAFT_02625 | UDP-3-O-acyl N-acetylglucosamine deacetylase   | 1.251  | 0.317  |
| DespoDRAFT_02626 | hypothetical protein   | -1.374 | 0.649  |
| DespoDRAFT_02627 | PAS domain S-box   | -1.089 | 0.922  |
| DespoDRAFT_02628 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains     | 1.272  | 0.418  |
| DespoDRAFT_02629 | RNA methyltransferase RsmD family  | 1.913  | 0.672  |
| DespoDRAFT_02630 | pantetheine-phosphate adenyltransferase  | 2.746  | 0.275  |
| DespoDRAFT_02631 | transcriptional regulator  | 1.535  | 0.128  |
| DespoDRAFT_02632 | N-methylhydantoinase A/acetone carboxylase beta subunit                                | -1.443 | 0.0946 |
| DespoDRAFT_02633 | deacetylase histone deacetylase/acetoin utilization protein                            | -1.433 | 0.316  |
| DespoDRAFT_02634 | lysyl-tRNA synthetase-like protein GenX  | -1.17  | 0.773  |
| DespoDRAFT_02635 | HD-GYP domain-containing protein   | 1.221  | 0.54   |
| DespoDRAFT_02636 | Fe-S oxidoreductase  | 1.911  | 0.125  |
| DespoDRAFT_02637 | argininosuccinate synthase   | 2.676  | 0.0225 |
| DespoDRAFT_02638 | hypothetical protein   | -1.163 | 0.607  |
| DespoDRAFT_02639 | hypothetical protein   | -3     | 0.268  |
| DespoDRAFT_02640 | putative transcriptional regulator   | -2.293 | 0.079  |
| DespoDRAFT_02641 | hypothetical protein   | -2.67  | 0.0588 |
| DespoDRAFT_02642 | translation elongation factor P/translation initiation factor 5A                       | 4.23   | 0.102  |
| DespoDRAFT_02643 | inorganic pyrophosphatase/exopolyphosphatase   | 1.127  | 0.79   |
| DespoDRAFT_02644 | pyruvate/2-oxoglutarate dehydrogenase complex dihydrolipoamide dehydrogenase component | -1.14  | 0.608  |
| DespoDRAFT_02645 | isoleucine patch superfamily enzyme carbonic anhydrase/acetyltransferase               | 1.275  | 0.298  |
| DespoDRAFT_02646 | hypothetical protein   | 4.98   | 0.0339 |
| DespoDRAFT_02647 | Na <sup>+</sup> /H <sup>+</sup> antiporter NhaD-like permease                          | -1.36  | 0.47   |
| DespoDRAFT_02648 | exonuclease DNA polymerase III epsilon subunit family                                  | -2.198 | 0.471  |
| DespoDRAFT_02650 | Protein of unknown function (DUF3375)  | -1.847 | 0.0852 |
| DespoDRAFT_02651 | hypothetical protein   | -1.744 | 0.401  |
| DespoDRAFT_02652 | hypothetical protein   | -1.875 | 0.0592 |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_02653 | hypothetical protein   | -1.585 | 0.411  |
| DespoDRAFT_02655 | hypothetical protein   | -1.005 | 0.964  |
| DespoDRAFT_02656 | cupin domain-containing protein  | -1.016 | 0.935  |
| DespoDRAFT_02657 | hypothetical protein   | 1.361  | NaN    |
| DespoDRAFT_02658 | IS66 Orf2 like protein   | -1.712 | NaN    |
| DespoDRAFT_02660 | transposase family protein   | -1.63  | 0.606  |
| DespoDRAFT_02661 | hypothetical protein   | -1.55  | 0.0952 |
| DespoDRAFT_02662 | putative periplasmic or secreted lipoprotein   | -1.096 | 0.88   |
| DespoDRAFT_02663 | hypothetical protein   | 1.22   | 0.791  |
| DespoDRAFT_02664 | site-specific recombinase XerD   | -2.063 | 0.345  |
| DespoDRAFT_02666 | hypothetical protein   | -2.953 | 0.221  |
| DespoDRAFT_02667 | hypothetical protein   | -1.73  | 0.229  |
| DespoDRAFT_02671 | Mn-dependent transcriptional regulator   | 1.795  | 0.103  |
| DespoDRAFT_02672 | ATP-dependent protease La  | 1.374  | 0.0586 |
| DespoDRAFT_02673 | sugar kinase ribokinase  | 5.501  | 0.128  |
| DespoDRAFT_02674 | S-adenosylmethionine synthetase  | 3.861  | 0.0315 |
| DespoDRAFT_02675 | adenosylhomocysteinase   | 3.689  | 0.0254 |
| DespoDRAFT_02676 | hypothetical protein   | -1.798 | 0.0484 |
| DespoDRAFT_02677 | radical SAM superfamily enzyme<br>dinitrogenase iron-molybdenum cofactor<br>biosynthesis protein | -6.03  | 0.0797 |
| DespoDRAFT_02678 | glycosidase  | -3.775 | 0.086  |
| DespoDRAFT_02679 | sugar kinase ribokinase  | -7.227 | 0.122  |
| DespoDRAFT_02680 | HAD-superfamily hydrolase subfamily IIB  | -8.802 | 0.0226 |
| DespoDRAFT_02681 | HAD-superfamily hydrolase subfamily IIB  | -6.045 | 0.058  |
| DespoDRAFT_02682 | exopolyphosphatase   | 1.556  | 0.23   |
| DespoDRAFT_02683 | Ribbon-helix-helix protein copG family   | -1.441 | 0.478  |
| DespoDRAFT_02684 | hypothetical protein   | -1.281 | 0.227  |
| DespoDRAFT_02685 | ATPase involved in chromosome<br>partitioning  | -1.202 | 0.317  |
| DespoDRAFT_02686 | hypothetical protein   | -1.199 | 0.553  |
| DespoDRAFT_02687 | Pyruvate ferredoxin oxidoreductase   | -1.564 | 0.155  |
| DespoDRAFT_02688 | Pyruvate ferredoxin oxidoreductase   | -1.167 | 0.126  |
| DespoDRAFT_02689 | alpha-hydroxyacid dehydrogenase FMN-<br>dependent L-lactate dehydrogenase                        | 1.07   | 0.488  |
| DespoDRAFT_02691 | hypothetical protein   | -1.167 | 0.332  |
| DespoDRAFT_02692 | nucleoside-diphosphate-sugar epimerase   | 1.4    | 0.307  |
| DespoDRAFT_02693 | aminopeptidase N   | -1.413 | 0.134  |
| DespoDRAFT_02694 | uncharacterized protein involved in an early<br>stage of isoprenoid biosynthesis                 | -1.766 | 0.0997 |
| DespoDRAFT_02695 | nucleotide sugar dehydrogenase   | -1.976 | 0.118  |
| DespoDRAFT_02696 | hypothetical protein   | -4.332 | 0.0636 |
| DespoDRAFT_02697 | KamA family protein  | -1.713 | 0.107  |
| DespoDRAFT_02699 | putative O-methyltransferase   | 1.675  | 0.193  |
| DespoDRAFT_02700 | putative RNA-binding protein containing  | -1.11  | 0.619  |

|                  |   |        |        |
|------------------|---|--------|--------|
|                  | Zn ribbon   |        |        |
| DespoDRAFT_02701 | HflK protein  | 1.764  | 0.0743 |
| DespoDRAFT_02702 | HflC protein  | 1.425  | 0.145  |
| DespoDRAFT_02703 | protein of unknown function (DUF1713)                                       | -1.312 | 0.457  |
| DespoDRAFT_02704 | hypothetical protein  | -1.316 | 0.672  |
| DespoDRAFT_02705 | putative regulatory protein FmdB family                                     | 1.068  | 0.722  |
| DespoDRAFT_02706 | Co-chaperonin GroES   | 2.431  | 0.0551 |
| DespoDRAFT_02707 | chaperonin GroL   | 1.706  | 0.0586 |
| DespoDRAFT_02708 | TolQ protein  | 1.54   | 0.041  |
| DespoDRAFT_02709 | TolR protein  | 1.313  | 0.18   |
| DespoDRAFT_02710 | TolA protein  | -1.004 | 0.982  |
| DespoDRAFT_02711 | tol-pal system beta propeller repeat protein TolB                           | 2.375  | 0.0679 |
| DespoDRAFT_02712 | peptidoglycan-associated lipoprotein  | 1.503  | 0.148  |
| DespoDRAFT_02713 | tol-pal system protein YbgF   | 1.114  | 0.412  |
| DespoDRAFT_02714 | holliday junction resolvasome, endonuclease subunit                         | -1.03  | 0.842  |
| DespoDRAFT_02715 | holliday junction resolvasome DNA-binding subunit                           | -1.092 | 0.534  |
| DespoDRAFT_02716 | Holliday junction DNA helicase RuvB subunit                                 | 1.607  | 0.099  |
| DespoDRAFT_02717 | ribosomal protein L13 bacterial type  | 2.649  | 0.111  |
| DespoDRAFT_02718 | ribosomal protein S9  | 2.261  | 0.0841 |
| DespoDRAFT_02719 | exonuclease I   | 1.199  | 0.18   |
| DespoDRAFT_02720 | bacterial nucleoid DNA-binding protein                                      | 1.406  | 0.42   |
| DespoDRAFT_02721 | putative inhibitor of MCP methylation CheC                                  | -1.386 | 0.298  |
| DespoDRAFT_02722 | Zn-dependent hydrolase glyoxylase   | -1.015 | 0.873  |
| DespoDRAFT_02723 | peroxiredoxin   | -2.43  | 0.0243 |
| DespoDRAFT_02724 | putative peroxiredoxin  | -2.079 | 0.0681 |
| DespoDRAFT_02725 | prepilin signal peptidase PulO-like peptidase                               | 1.427  | 0.283  |
| DespoDRAFT_02726 | ATP-dependent protease La   | 1.556  | 0.0869 |
| DespoDRAFT_02727 | universal bacterial protein YeaZ  | 1.428  | 0.354  |
| DespoDRAFT_02728 | phosphatidylserine decarboxylase precursor-related protein                  | -1.141 | 0.438  |
| DespoDRAFT_02729 | transcription elongation factor GreA  | 1.02   | 0.924  |
| DespoDRAFT_02730 | DNA-directed RNA polymerase omega subunit                                   | 1.005  | 0.986  |
| DespoDRAFT_02731 | putative ATPase of the PP-loop superfamily implicated in cell cycle control | -1.106 | 0.819  |
| DespoDRAFT_02732 | TIGR00294 family protein  | -1.47  | 0.145  |
| DespoDRAFT_02733 | D-alanyl-D-alanine carboxypeptidase (penicillin-binding protein 4)          | -1.264 | 0.721  |
| DespoDRAFT_02734 | hypothetical protein  | -1.719 | 0.494  |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_02735 | hypothetical protein   | -3.402 | 0.104  |
| DespoDRAFT_02736 | flagellar motor protein  | -1.964 | 0.0947 |
| DespoDRAFT_02737 | glucose-1-phosphate thymidyltransferase short form                                 | 1.155  | 0.228  |
| DespoDRAFT_02738 | dTDP-4-dehydrorhamnose 3 5-epimerase   | 1.068  | 0.935  |
| DespoDRAFT_02739 | dTDP-4-dehydrorhamnose reductase   | 1.416  | 0.364  |
| DespoDRAFT_02740 | ABC-type uncharacterized transport system periplasmic component                    | 1.751  | 0.0709 |
| DespoDRAFT_02741 | signal transduction histidine kinase   | 2.009  | 0.321  |
| DespoDRAFT_02742 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains | -1.194 | 0.0331 |
| DespoDRAFT_02743 | outer membrane cobalamin receptor protein  | 1.179  | 0.685  |
| DespoDRAFT_02744 | putative nucleoside-diphosphate sugar epimerase                                    | 1.478  | 0.222  |
| DespoDRAFT_02745 | General secretion pathway protein K  | -4.044 | 0.172  |
| DespoDRAFT_02758 | hypothetical protein   | 1.498  | 0.864  |
| DespoDRAFT_02759 | hypothetical protein   | -1.419 | 0.385  |
| DespoDRAFT_02761 | TIGR00268 family protein   | -1.64  | 0.0752 |
| DespoDRAFT_02762 | nucleoside diphosphate kinase  | 8      | 0.0904 |
| DespoDRAFT_02763 | dephospho-CoA kinase   | 1.042  | 0.886  |
| DespoDRAFT_02764 | transcription termination factor Rho   | -1.069 | 0.461  |
| DespoDRAFT_02765 | ribosomal protein L31  | 1.71   | 0.169  |
| DespoDRAFT_02766 | peptide chain release factor 1   | 2.016  | 0.0631 |
| DespoDRAFT_02767 | protein-(glutamine-N5) methyltransferase release factor-specific                   | 1.462  | 0.152  |
| DespoDRAFT_02768 | ribosomal protein S2   | 1.281  | 0.104  |
| DespoDRAFT_02769 | translation elongation factor Ts   | 1.193  | 0.259  |
| DespoDRAFT_02770 | uridylate kinase   | 1.666  | 0.113  |
| DespoDRAFT_02771 | ribosome recycling factor  | 1.795  | 0.101  |
| DespoDRAFT_02772 | undecaprenyl diphosphate synthase  | 1.393  | 0.275  |
| DespoDRAFT_02773 | CDP-diglyceride synthetase   | 1.781  | 0.0823 |
| DespoDRAFT_02774 | 1-deoxy-D-xylulose 5-phosphate reductoisomerase                                    | 2.016  | 0.172  |
| DespoDRAFT_02775 | putative membrane-associated Zn-dependent protease                                 | 1.904  | 0.112  |
| DespoDRAFT_02776 | phosphoribosylformylglycinamide (FGAM) synthase synthetase domain                  | 1.324  | 0.0604 |
| DespoDRAFT_02777 | phosphoribosylformylglycinamide (FGAM) synthase glutamine amidotransferase domain  | 1.463  | 0.528  |
| DespoDRAFT_02778 | putative endoIII-related endonuclease  | 1.99   | 0.0339 |
| DespoDRAFT_02779 | proline dehydrogenase  | 1.319  | 0.435  |
| DespoDRAFT_02781 | hypothetical protein   | 1.335  | 0.631  |



|                  |  |        |         |
|------------------|--|--------|---------|
| DespoDRAFT_02782 | PEP-CTERM putative exosortase interaction domain-containing protein        | 1.4    | 0.405   |
| DespoDRAFT_02783 | hypothetical protein   | -1.378 | 0.222   |
| DespoDRAFT_02784 | hypothetical protein   | 1.104  | 0.651   |
| DespoDRAFT_02785 | DNA segregation ATPase FtsK/SpoIIIE family                                 | 1.36   | 0.494   |
| DespoDRAFT_02786 | putative O-methyltransferase   | 1.155  | 0.692   |
| DespoDRAFT_02787 | uncharacterized iron-regulated protein                                     | 1.194  | 0.166   |
| DespoDRAFT_02788 | hypothetical protein   | -1.806 | 0.0674  |
| DespoDRAFT_02791 | hypothetical protein   | 1.589  | 0.173   |
| DespoDRAFT_02792 | arginyl-tRNA synthetase  | 1.443  | 0.217   |
| DespoDRAFT_02793 | cell division protein  | -1.171 | 0.35    |
| DespoDRAFT_02794 | glutamyl-tRNA(Gln) and/or aspartyl-tRNA(Asn) amidotransferase C subunit    | 2.308  | 0.0418  |
| DespoDRAFT_02795 | glutamyl-tRNA(Gln) and/or aspartyl-tRNA(Asn) amidotransferase A subunit    | 1.479  | 0.286   |
| DespoDRAFT_02796 | hypothetical protein   | 2.547  | 0.182   |
| DespoDRAFT_02797 | hypothetical protein   | 2.551  | 0.194   |
| DespoDRAFT_02798 | DNA mismatch repair protein MutL   | 4.668  | 0.184   |
| DespoDRAFT_02799 | uncharacterized protein involved in formation of curli polymers            | 2.384  | 0.0231  |
| DespoDRAFT_02800 | hypothetical protein   | -1.27  | 0.144   |
| DespoDRAFT_02801 | transposase  | 1.147  | 0.433   |
| DespoDRAFT_02802 | PAS domain S-box   | -1.037 | 0.544   |
| DespoDRAFT_02803 | hypothetical protein   | -27.97 | 0.00749 |
| DespoDRAFT_02805 | adenylosuccinate synthase  | 1.042  | 0.629   |
| DespoDRAFT_02806 | cytosine/adenosine deaminase   | 2.046  | 0.112   |
| DespoDRAFT_02807 | glutamate-1-semialdehyde-2, 1-aminomutase                                  | 1.559  | 0.046   |
| DespoDRAFT_02808 | UDP-N-acetylmuramate:L-alanyl-gamma-D-glutamyl-meso-diaminopimelate ligase | 1.412  | 0.128   |
| DespoDRAFT_02809 | hypothetical protein   | 2.075  | 0.229   |
| DespoDRAFT_02810 | hemerythrin-like metal-binding domain-containing protein                   | 1.468  | 0.0811  |
| DespoDRAFT_02811 | hypothetical protein   | 1.152  | 0.598   |
| DespoDRAFT_02812 | exodeoxyribonuclease V alpha subunit                                       | 1.048  | 0.855   |
| DespoDRAFT_02813 | ResB protein required for cytochrome c biosynthesis                        | 1.343  | 0.0453  |
| DespoDRAFT_02814 | cytochrome c-type biogenesis protein CcsB                                  | 2.55   | 0.166   |
| DespoDRAFT_02815 | QrcA class III cytochrome C family protein                                 | 2.754  | 0.0413  |
| DespoDRAFT_02816 | QrcB anaerobic dehydrogenase typically selenocysteine-containing           | 2.341  | 0.0354  |
| DespoDRAFT_02817 | QrcC Fe-S-cluster-containing hydrogenase subunit                           | 3.301  | 0.0408  |
| DespoDRAFT_02818 | QrcD protein / polysulfide reductase                                       | 3.166  | 0.0268  |

|                  |   |         |        |
|------------------|---|---------|--------|
| DespoDRAFT_02819 | hypothetical protein  | 1.75    | 0.157  |
| DespoDRAFT_02820 | pilus biosynthesis protein HicB   | -5.998  | 0.029  |
| DespoDRAFT_02821 | putative nucleic-acid-binding protein                                   | -1.578  | 0.0863 |
| DespoDRAFT_02822 | hypothetical protein  | -2.001  | 0.0708 |
| DespoDRAFT_02823 | Protein of unknown function (DUF1703)                                   | -3.261  | 0.0569 |
| DespoDRAFT_02824 | putative transcription regulator containing HTH domain                  | -3.075  | 0.0605 |
| DespoDRAFT_02825 | hypothetical protein  | -2.368  | 0.103  |
| DespoDRAFT_02826 | hypothetical protein  | -1.119  | 0.59   |
| DespoDRAFT_02827 | integrase family protein  | -1.827  | 0.486  |
| DespoDRAFT_02828 | DNA replication protein   | -1.563  | NaN    |
| DespoDRAFT_02831 | growth inhibitor  | -2.293  | 0.389  |
| DespoDRAFT_02832 | hypothetical protein  | -4.719  | 0.2    |
| DespoDRAFT_02833 | putative transcription regulator containing HTH domain                  | -1.422  | 0.75   |
| DespoDRAFT_02835 | Transposase IS66 family   | 1.418   | 0.402  |
| DespoDRAFT_02836 | hypothetical protein  | 1.324   | 0.661  |
| DespoDRAFT_02837 | putative PLP-dependent enzyme possibly involved in cell wall biogenesis | 1.006   | 0.985  |
| DespoDRAFT_02839 | endonuclease IV   | 1.237   | 0.818  |
| DespoDRAFT_02840 | acetyltransferase   | 1.206   | 0.627  |
| DespoDRAFT_02841 | N-acetylneuraminate synthase  | -1.186  | 0.435  |
| DespoDRAFT_02842 | CMP-N-acetylneuraminic acid synthetase                                  | -1.139  | 0.759  |
| DespoDRAFT_02843 | methyltransferase family protein  | -1.179  | 0.749  |
| DespoDRAFT_02844 | Fe-S oxidoreductase   | -1.155  | 0.91   |
| DespoDRAFT_02845 | flagellin/flagellar hook associated protein                             | -2.089  | 0.157  |
| DespoDRAFT_02846 | flagellar capping protein   | -1.237  | 0.773  |
| DespoDRAFT_02847 | flagellar biosynthetic protein FliS                                     | -1.008  | 0.993  |
| DespoDRAFT_02848 | hypothetical protein  | -1.967  | 0.494  |
| DespoDRAFT_02849 | flagellar protein FlaG  | -1.322  | 0.171  |
| DespoDRAFT_02850 | hypothetical protein  | #VALUE! | NaN    |
| DespoDRAFT_02851 | flagellar hook capping protein  | -7.839  | 0.0635 |
| DespoDRAFT_02852 | flagellar hook-basal body protein                                       | -4.173  | 0.0131 |
| DespoDRAFT_02853 | flagellar hook-associated protein FlgK                                  | -3.761  | 0.166  |
| DespoDRAFT_02854 | flagellar hook-associated protein 3                                     | -3.934  | 0.108  |
| DespoDRAFT_02855 | hypothetical protein  | -2.001  | 0.0381 |
| DespoDRAFT_02856 | glutamyl-tRNA(Gln) and/or aspartyl-tRNA(Asn) amidotransferase B subunit | 1.472   | 0.298  |
| DespoDRAFT_02857 | hypothetical protein  | 1.094   | 0.901  |
| DespoDRAFT_02858 | S-adenosylmethionine:tRNA ribosyltransferase-isomerase                  | 1.04    | 0.841  |
| DespoDRAFT_02859 | tRNA-guanine transglycosylase queuosine-34-forming                      | -1.101  | 0.701  |
| DespoDRAFT_02860 | hydrogenase nickel insertion protein HypA                               | -1.54   | 0.107  |
| DespoDRAFT_02861 | hydrogenase accessory protein HypB                                      | -1.222  | 0.337  |

|                  |   |        |        |
|------------------|---|--------|--------|
| DespoDRAFT_02862 | putative dioxygenase  | -1.416 | 0.54   |
| DespoDRAFT_02863 | SprT-like family  | 1.482  | 0.201  |
| DespoDRAFT_02864 | NAD-dependent protein deacetylase SIR2 family                         | 2.45   | 0.155  |
| DespoDRAFT_02865 | YeeE/YedE family protein (DUF395)                                     | -1.478 | 0.22   |
| DespoDRAFT_02866 | YeeE/YedE family protein (DUF395)                                     | -1.545 | 0.0537 |
| DespoDRAFT_02867 | diacylglycerol kinase   | -1.511 | 0.267  |
| DespoDRAFT_02868 | hypothetical protein  | 1.498  | 0.294  |
| DespoDRAFT_02869 | putative xylanase/chitin deacetylase                                  | 1.166  | 0.353  |
| DespoDRAFT_02870 | glutamyl-tRNA synthetase  | 5.392  | 0.0487 |
| DespoDRAFT_02871 | ribosomal protein L32   | 5.356  | 0.0728 |
| DespoDRAFT_02872 | acyl carrier protein  | 4.103  | 0.0483 |
| DespoDRAFT_02873 | ribose 5-phosphate isomerase B  | 2.78   | 0.0846 |
| DespoDRAFT_02874 | glycine/serine hydroxymethyltransferase                               | 2.192  | 0.073  |
| DespoDRAFT_02875 | deoxycytidylate deaminase   | 2.489  | 0.113  |
| DespoDRAFT_02876 | transcriptional regulator NrdR  | 2.382  | 0.0838 |
| DespoDRAFT_02877 | riboflavin biosynthesis protein RibD                                  | 1.368  | 0.155  |
| DespoDRAFT_02878 | riboflavin synthase alpha subunit                                     | 1.266  | 0.231  |
| DespoDRAFT_02879 | GTP cyclohydrolase II/3 4-dihydroxy-2-butanone 4-phosphate synthase   | 1.756  | 0.119  |
| DespoDRAFT_02880 | 6, 7-dimethyl-8-ribityllumazine synthase                              | 1.339  | 0.084  |
| DespoDRAFT_02881 | transcription antitermination factor NusB                             | 1.701  | 0.0354 |
| DespoDRAFT_02882 | Zn-dependent hydrolase glyoxylase                                     | 1.31   | 0.157  |
| DespoDRAFT_02884 | Protein of unknown function (DUF1573)                                 | 3.146  | 0.0823 |
| DespoDRAFT_02885 | haloacid dehalogenase superfamily enzyme subfamily IA                 | 2.229  | 0.114  |
| DespoDRAFT_02886 | sat ATP sulphurylase  | 1.401  | 0.172  |
| DespoDRAFT_02887 | Sulfate (and Phosphate) permease                                      | 1.453  | 0.0982 |
| DespoDRAFT_02888 | putative S-adenosylmethionine-dependent methyltransferase YraL family | 2.624  | 0.468  |
| DespoDRAFT_02889 | putative endonuclease related to Holliday junction resolvase          | 7.383  | 0.0901 |
| DespoDRAFT_02890 | ribonuclease HII  | 3.128  | 0.108  |
| DespoDRAFT_02891 | ribosomal protein L19   | 3.537  | 0.053  |
| DespoDRAFT_02892 | hypothetical protein  | 2.748  | 0.0381 |
| DespoDRAFT_02893 | tRNA (guanine-N1)-methyltransferase                                   | 2.441  | 0.0728 |
| DespoDRAFT_02894 | 16S rRNA processing protein RimM                                      | 1.952  | 0.176  |
| DespoDRAFT_02895 | putative RNA-binding protein (contains KH domain)                     | 1.773  | 0.146  |
| DespoDRAFT_02896 | ribosomal protein S16   | 2.795  | 0.0336 |
| DespoDRAFT_02897 | signal recognition particle protein                                   | 2.141  | 0.0414 |
| DespoDRAFT_02898 | 23S rRNA m2A2503 methyltransferase                                    | -1.162 | 0.399  |
| DespoDRAFT_02899 | growth inhibitor  | -1.788 | 0.0241 |
| DespoDRAFT_02900 | growth regulator  | -1.082 | 0.514  |

|                  |   |         |        |
|------------------|---|---------|--------|
| DespoDRAFT_02901 | putative tRNA(5-methylaminomethyl-2-thiouridylate) methyltransferase with PP-loop ATPase domain | 5.026   | 0.228  |
| DespoDRAFT_02902 | coenzyme F390 synthetase  | 1.5     | 0.194  |
| DespoDRAFT_02903 | ABC-type branched-chain amino acid transport system ATPase component                            | 1.707   | 0.0932 |
| DespoDRAFT_02904 | ABC-type branched-chain amino acid transport system ATPase component                            | 1.179   | 0.592  |
| DespoDRAFT_02905 | ABC-type branched-chain amino acid transport system permease component                          | 1.387   | 0.653  |
| DespoDRAFT_02906 | branched-chain amino acid ABC-type transport system permease component                          | 1.629   | 0.108  |
| DespoDRAFT_02907 | ABC-type branched-chain amino acid transport system periplasmic component                       | 1.757   | 0.0998 |
| DespoDRAFT_02908 | Malate oxidoreductase   | -1.833  | 0.132  |
| DespoDRAFT_02909 | succinate dehydrogenase Gamma subunit   | 1.695   | 0.103  |
| DespoDRAFT_02910 | succinate dehydrogenase a subunit   | 1.854   | 0.083  |
| DespoDRAFT_02911 | succinate dehydrogenase Beta subunit  | 1.542   | 0.108  |
| DespoDRAFT_02912 | hypothetical protein  | 1.115   | 0.547  |
| DespoDRAFT_02913 | putative signal-transduction protein containing cAMP-binding and CBS domains                    | -1.058  | 0.882  |
| DespoDRAFT_02914 | Cache domain protein  | 1.891   | 0.271  |
| DespoDRAFT_02916 | Transposase IS66 family   | #VALUE! | NaN    |
| DespoDRAFT_02917 | hypothetical protein  | -29.501 | 0.0466 |
| DespoDRAFT_02918 | hypothetical protein  | -7.582  | 0.0951 |
| DespoDRAFT_02919 | hypothetical protein  | -1.722  | 0.702  |
| DespoDRAFT_02920 | hypothetical protein  | 2.681   | 0.346  |
| DespoDRAFT_02921 | ActP acetate permease / putative symporter  | 1.789   | 0.496  |
| DespoDRAFT_02922 | hypothetical protein  | 1.618   | 0.659  |
| DespoDRAFT_02923 | dynamain family protein   | 1.525   | 0.194  |
| DespoDRAFT_02924 | formate/nitrite transporter family protein  | 1.104   | 0.816  |
| DespoDRAFT_02925 | hypothetical protein  | 1.124   | 0.596  |
| DespoDRAFT_02926 | putative membrane protein   | -3.22   | 0.0802 |
| DespoDRAFT_02927 | transposase family protein  | -3.859  | 0.0559 |
| DespoDRAFT_02928 | PAS domain S-box  | -1.037  | 0.888  |
| DespoDRAFT_02929 | hypothetical protein  | 1.119   | NaN    |
| DespoDRAFT_02932 | FAD/FMN-dependent dehydrogenase   | 1.667   | 0.106  |
| DespoDRAFT_02933 | Fe-S oxidoreductase   | -1.114  | 0.341  |
| DespoDRAFT_02934 | putative membrane protein   | -3.379  | 0.112  |
| DespoDRAFT_02935 | succinyl-CoA synthetase, alpha subunit  | -2.705  | 0.104  |
| DespoDRAFT_02936 | succinyl-CoA synthetase, beta subunit   | -1.224  | 0.186  |
| DespoDRAFT_02937 | hypothetical protein  | -2.183  | 0.114  |
| DespoDRAFT_02938 | Protein of unknown function (DUF3478)   | -1.348  | 0.454  |
| DespoDRAFT_02939 | hypothetical protein  | -1.12   | 0.745  |
| DespoDRAFT_02940 | hypothetical protein  | 1.256   | 0.619  |

|                  |   |        |         |
|------------------|---|--------|---------|
| DespoDRAFT_02941 | hypothetical protein  | -1.049 | 0.763   |
| DespoDRAFT_02942 | CRISPR-associated protein Cas2  | -1.311 | 0.26    |
| DespoDRAFT_02943 | CRISPR-associated endonuclease Cas1   | -1.199 | 0.172   |
| DespoDRAFT_02944 | CRISPR-associated protein Cas5  | -1.122 | 0.365   |
| DespoDRAFT_02945 | CRISPR-associated protein Cas7/Cse4/CasC  | 1.022  | 0.583   |
| DespoDRAFT_02946 | CRISPR-associated protein Cas6/Cse3/CasE  | -1.101 | 0.0709  |
| DespoDRAFT_02947 | CRISPR type I-E protein CasB  | -1.132 | 0.427   |
| DespoDRAFT_02948 | CRISPR type I-E protein CasA  | -1.704 | 0.101   |
| DespoDRAFT_02949 | CRISPR-associated helicase Cas3/CRISPR-associated endonuclease Cas3-HD                  | -1.621 | 0.136   |
| DespoDRAFT_02950 | hypothetical protein  | -1.743 | 0.327   |
| DespoDRAFT_02951 | putative Zn peptidase   | -1.849 | 0.113   |
| DespoDRAFT_02952 | succinate-semialdehyde dehydrogenase  | -1.506 | 0.0915  |
| DespoDRAFT_02953 | TRAP transporter solute receptor TAXI family  | -2.279 | 0.0676  |
| DespoDRAFT_02954 | type II secretory pathway component ExeA (predicted ATPase)                             | -3.669 | 0.212   |
| DespoDRAFT_02955 | glyceraldehyde-3-phosphate dehydrogenase/erythrose-4-phosphate dehydrogenase            | 1.387  | 0.647   |
| DespoDRAFT_02956 | formyltetrahydrofolate synthetase   | 1.364  | 0.227   |
| DespoDRAFT_02957 | 5, 10-methylene-tetrahydrofolate dehydrogenase/methenyl tetrahydrofolate cyclohydrolase | 1.873  | 0.201   |
| DespoDRAFT_02958 | protein of unknown function (DUF1844)   | 1.197  | 0.691   |
| DespoDRAFT_02959 | 4-diphosphocytidyl-2C-methyl-D-erythritol kinase  | 1.469  | 0.319   |
| DespoDRAFT_02961 | ribose-phosphate pyrophosphokinase  | 1.506  | 0.158   |
| DespoDRAFT_02962 | ribosomal protein L25 Ctc-form  | 1.583  | 0.112   |
| DespoDRAFT_02963 | peptidyl-tRNA hydrolase   | 1.429  | 0.117   |
| DespoDRAFT_02964 | CarD-like transcriptional regulator   | 1.332  | 0.346   |
| DespoDRAFT_02965 | pseudouridine synthase RluA family  | 1.248  | 0.622   |
| DespoDRAFT_02966 | RNA methyltransferase TrmH family group 1   | 2.016  | 0.525   |
| DespoDRAFT_02967 | D-tyrosyl-tRNA(Tyr) deacylase   | -1.926 | 0.701   |
| DespoDRAFT_02968 | histidinol phosphate phosphatase HisJ family  | 2.398  | 0.455   |
| DespoDRAFT_02969 | glycosyltransferase   | -1.174 | 0.893   |
| DespoDRAFT_02970 | ATP-dependent chaperone ClpB  | -1.6   | 0.0626  |
| DespoDRAFT_02971 | PAS domain S-box  | -1.822 | 0.0952  |
| DespoDRAFT_02972 | ferredoxin  | -3.432 | 0.00355 |
| DespoDRAFT_02973 | hypothetical protein  | -4.767 | 0.0205  |
| DespoDRAFT_02974 | hypothetical protein  | -5.456 | 0.0452  |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_02975 | transglutaminase-like enzyme predicted cysteine protease                       | -1.506 | 0.651  |
| DespoDRAFT_02976 | PAS domain S-box   | -1.036 | 0.844  |
| DespoDRAFT_02977 | histidine kinase Response regulator receiver domain protein histidine kinase   | -1.833 | 0.359  |
| DespoDRAFT_02978 | phosphoenolpyruvate-protein phosphotransferase                                 | -1.032 | 0.923  |
| DespoDRAFT_02979 | hypothetical protein   | -1.524 | 0.731  |
| DespoDRAFT_02980 | PAS domain-containing protein  | 1.27   | NaN    |
| DespoDRAFT_02981 | diguanylate cyclase (GGDEF) domain-containing protein                          | -1.495 | 0.679  |
| DespoDRAFT_02984 | integrase family protein   | -1.575 | 0.733  |
| DespoDRAFT_02985 | hypothetical protein   | -2.166 | 0.0794 |
| DespoDRAFT_02986 | outer membrane protein/peptidoglycan-associated (lipo)protein                  | -1.763 | 0.178  |
| DespoDRAFT_02987 | response regulator containing a CheY-like receiver domain and an HD-GYP domain | 1.151  | 0.787  |
| DespoDRAFT_02990 | Retron-type reverse transcriptase  | 1.663  | 0.0777 |
| DespoDRAFT_02992 | nuclease-like protein  | -1.808 | 0.329  |
| DespoDRAFT_02993 | ABC-type antimicrobial peptide transport system permease component             | -1.599 | 0.0861 |
| DespoDRAFT_02994 | ABC-type antimicrobial peptide transport system ATPase component               | -1.149 | 0.852  |
| DespoDRAFT_02995 | RND family efflux transporter  | -1.071 | 0.884  |
| DespoDRAFT_02996 | efflux transporter outer membrane factor lipoprotein NodT family               | -1.126 | 0.815  |
| DespoDRAFT_02997 | hypothetical protein   | -1.634 | 0.615  |
| DespoDRAFT_02998 | hypothetical protein   | 1.782  | 0.0215 |
| DespoDRAFT_02999 | hypothetical protein   | -8.894 | 0.0474 |
| DespoDRAFT_03000 | hypothetical protein   | -1.101 | 0.625  |
| DespoDRAFT_03001 | acetyl-CoA carboxylase carboxyltransferase component (subunits alpha and beta) | -1.016 | 0.751  |
| DespoDRAFT_03002 | hypothetical protein   | 1.437  | 0.489  |
| DespoDRAFT_03003 | pyruvate/oxaloacetate carboxyltransferase                                      | 1.276  | 0.218  |
| DespoDRAFT_03004 | hypothetical protein   | -1.569 | 0.0841 |
| DespoDRAFT_03006 | hypothetical protein   | -1.036 | 0.777  |
| DespoDRAFT_03007 | 2, 3-bisphosphoglycerate-independent phosphoglycerate mutase                   | -1     | 0.994  |
| DespoDRAFT_03008 | iojap-like ribosome-associated protein   | -1.337 | 0.596  |
| DespoDRAFT_03009 | nicotinate/nicotinamide nucleotide adenylyltransferase                         | 1.809  | 0.514  |
| DespoDRAFT_03010 | Obg family GTPase CgtA   | -2.029 | 0.122  |
| DespoDRAFT_03011 | ribosomal protein L27  | 1.85   | 0.0675 |
| DespoDRAFT_03012 | ribosomal protein L21  | 3.154  | 0.116  |

|                  |  |        |         |
|------------------|--|--------|---------|
| DespoDRAFT_03013 | alkylphosphonate utilization operon protein PhnA                                       | 1.612  | 0.0704  |
| DespoDRAFT_03014 | hypothetical protein   | 1.154  | 0.562   |
| DespoDRAFT_03015 | dsrP   | 5.123  | 0.0175  |
| DespoDRAFT_03016 | dsrO, putative   | 4.233  | 0.0455  |
| DespoDRAFT_03017 | dsrJ; cytochrome c   | 4.652  | 0.0447  |
| DespoDRAFT_03018 | dsrK; Fe-S oxidoreductase  | 3.847  | 0.0218  |
| DespoDRAFT_03019 | dsrM   | 3.297  | 0.0556  |
| DespoDRAFT_03020 | hypothetical protein   | 3.588  | 0.0242  |
| DespoDRAFT_03021 | Lipid A 3-O-deacylase (PagL)   | 2.181  | 0.164   |
| DespoDRAFT_03022 | methylase involved in ubiquinone/menaquinone biosynthesis                              | 3.058  | 0.187   |
| DespoDRAFT_03023 | glycosyltransferase  | 1.884  | 0.349   |
| DespoDRAFT_03025 | folylpolyglutamate synthase/dihydrofolate synthase                                     | 3.782  | 0.00431 |
| DespoDRAFT_03026 | ribosomal protein S21  | 2.924  | 0.0355  |
| DespoDRAFT_03027 | adenylate kinase family protein  | 1.845  | 0.0464  |
| DespoDRAFT_03028 | DNA/RNA helicase superfamily I   | -2.58  | 0.337   |
| DespoDRAFT_03029 | Enolase  | 1.439  | 0.0138  |
| DespoDRAFT_03030 | CTP synthase   | 1.422  | 0.128   |
| DespoDRAFT_03031 | transcriptional regulator  | 1.583  | 0.44    |
| DespoDRAFT_03032 | N-methylhydantoinase B/acetone carboxylase alpha subunit                               | -1.257 | 0.431   |
| DespoDRAFT_03033 | putative methyltransferase YaeB/AF_0241 family   | -1.269 | 0.307   |
| DespoDRAFT_03034 | protein of unknown function (DUF1083)  | -1.13  | 0.529   |
| DespoDRAFT_03035 | 3-hydroxymyristoyl/3-hydroxydecanoyl-(acyl carrier protein) dehydratase                | 2.48   | 0.0801  |
| DespoDRAFT_03036 | polyketide synthase family protein   | 2.903  | 0.0482  |
| DespoDRAFT_03037 | PfaD family protein  | 1.643  | 0.193   |
| DespoDRAFT_03038 | ABC-type nitrate/sulfonate/bicarbonate/thiamine transport system ATPase component      | -1.835 | 0.132   |
| DespoDRAFT_03039 | ABC-type nitrate/sulfonate/bicarbonate transport/thiamine system permease component    | -2.542 | 0.0565  |
| DespoDRAFT_03040 | ABC-type nitrate/sulfonate/bicarbonate transport/thiamine system periplasmic component | -1.987 | 0.125   |
| DespoDRAFT_03041 | biotin synthase-like enzyme  | -1.482 | 0.186   |
| DespoDRAFT_03042 | rubrerythrin   | -1.122 | 0.43    |
| DespoDRAFT_03043 | Retron-type reverse transcriptase  | -1.128 | 0.221   |
| DespoDRAFT_03044 | transcription elongation factor  | -1.818 | 0.0812  |
| DespoDRAFT_03045 | Ribosomal protein S27  | -2.502 | 0.577   |
| DespoDRAFT_03046 | hypothetical protein   | -3.959 | 0.0904  |

|                  |   |         |        |
|------------------|---|---------|--------|
| DespoDRAFT_03047 | hypothetical protein  | -2.451  | 0.157  |
| DespoDRAFT_03051 | hypothetical protein  | 1.395   | 0.691  |
| DespoDRAFT_03053 | hypothetical protein  | -5.774  | 0.106  |
| DespoDRAFT_03054 | putative glycosyltransferase  | -14.387 | 0.42   |
| DespoDRAFT_03055 | putative glycosyltransferase  | -7.612  | 0.335  |
| DespoDRAFT_03056 | glycosyltransferase   | -5.695  | 0.289  |
| DespoDRAFT_03057 | hypothetical protein  | -6.455  | 0.194  |
| DespoDRAFT_03058 | hypothetical protein  | -6.252  | 0.341  |
| DespoDRAFT_03059 | hypothetical protein  | -5.057  | 0.104  |
| DespoDRAFT_03060 | hypothetical protein  | -2.417  | 0.0253 |
| DespoDRAFT_03061 | hypothetical protein  | -4.194  | 0.108  |
| DespoDRAFT_03063 | hypothetical protein  | -5.133  | 0.101  |
| DespoDRAFT_03064 | transposase IS605 OrfB family central region                          | -2.345  | 0.147  |
| DespoDRAFT_03065 | putative glycosyltransferase  | -2.413  | 0.136  |
| DespoDRAFT_03066 | hypothetical protein  | -2.897  | 0.116  |
| DespoDRAFT_03067 | glycosyltransferase   | -1.562  | 0.599  |
| DespoDRAFT_03068 | citrate synthase  | -2.031  | 0.148  |
| DespoDRAFT_03069 | glycosyl transferase  | -2.176  | 0.334  |
| DespoDRAFT_03070 | hypothetical protein  | -1.825  | 0.295  |
| DespoDRAFT_03071 | hypothetical protein  | -1.997  | 0.337  |
| DespoDRAFT_03073 | hypothetical protein  | -2.549  | 0.387  |
| DespoDRAFT_03075 | GDP-mannose 4 6-dehydratase   | -1.75   | 0.483  |
| DespoDRAFT_03076 | nucleoside-diphosphate-sugar epimerase                                | -2.058  | 0.525  |
| DespoDRAFT_03077 | mannose-1-phosphate guanylyltransferase/mannose-6-phosphate isomerase | -1.62   | 0.228  |
| DespoDRAFT_03078 | hypothetical protein  | -1.752  | 0.06   |
| DespoDRAFT_03079 | hypothetical protein  | -1.09   | 0.407  |
| DespoDRAFT_03085 | hypothetical protein  | -1.621  | 0.448  |
| DespoDRAFT_03086 | hypothetical protein  | -1.574  | 0.156  |
| DespoDRAFT_03087 | hypothetical protein  | -1.949  | 0.332  |
| DespoDRAFT_03088 | plasmid stability protein   | -1.241  | 0.538  |
| DespoDRAFT_03089 | putative nucleic acid-binding protein                                 | -1.351  | 0.514  |
| DespoDRAFT_03090 | hypothetical protein  | 1.204   | 0.0658 |
| DespoDRAFT_03091 | hypothetical protein  | -1.206  | 0.689  |
| DespoDRAFT_03092 | PemK-like protein   | -1.273  | 0.776  |
| DespoDRAFT_03093 | dTDP-D-glucose 4 6-dehydratase  | 2.176   | NaN    |
| DespoDRAFT_03095 | putative nucleotidyltransferase                                       | -1.178  | 0.823  |
| DespoDRAFT_03096 | hypothetical protein  | -1.201  | 0.458  |
| DespoDRAFT_03097 | dTDP-glucose 4 6-dehydratase  | -1.293  | 0.149  |
| DespoDRAFT_03098 | dTDP-4-dehydrorhamnose reductase                                      | -1.476  | 0.0989 |
| DespoDRAFT_03099 | glucose-1-phosphate thymidyltransferase short form                    | -1.151  | 0.484  |
| DespoDRAFT_03100 | dTDP-4-dehydrorhamnose 3, 5-epimerase                                 | -1.617  | 0.179  |



|                  |  |         |        |
|------------------|--|---------|--------|
| DespoDRAFT_03101 | methyltransferase family protein   | -1.099  | 0.714  |
| DespoDRAFT_03103 | hypothetical protein   | 1.526   | 0.61   |
| DespoDRAFT_03104 | hypothetical protein   | 2.162   | NaN    |
| DespoDRAFT_03105 | transposase  | -1.376  | 0.505  |
| DespoDRAFT_03106 | hypothetical protein   | -1.007  | NaN    |
| DespoDRAFT_03111 | apsK ATP sulphurylase/adenylylsulfate kinase                               | 6.229   | NaN    |
| DespoDRAFT_03112 | hypothetical protein   | -1.509  | 0.368  |
| DespoDRAFT_03113 | hypothetical protein   | -2.072  | 0.187  |
| DespoDRAFT_03114 | hypothetical protein   | -2.131  | 0.0981 |
| DespoDRAFT_03116 | putative membrane protein  | -1.839  | 0.249  |
| DespoDRAFT_03117 | nucleoside-diphosphate-sugar epimerase                                     | -2.488  | 0.442  |
| DespoDRAFT_03119 | putative transcriptional regulator with HTH domain                         | 1.697   | 0.443  |
| DespoDRAFT_03123 | hypothetical protein   | 1.497   | NaN    |
| DespoDRAFT_03124 | hypothetical protein   | -2.758  | 0.285  |
| DespoDRAFT_03126 | D-heptose-7- phosphate 1-kinase  | 2.348   | 0.112  |
| DespoDRAFT_03127 | phosphoserine phosphatase/homoserine phosphotransferase                    | 1.995   | 0.173  |
| DespoDRAFT_03128 | homoserine dehydrogenase   | 1.924   | 0.0253 |
| DespoDRAFT_03129 | phosphoribosylaminoimidazole synthetase                                    | -1.247  | 0.235  |
| DespoDRAFT_03130 | putative glycoprotease GCP   | -1.184  | 0.314  |
| DespoDRAFT_03131 | beta-glucosidase-like glycosyl hydrolase                                   | -1.494  | 0.157  |
| DespoDRAFT_03132 | DisA bacterial checkpoint controller nucleotide-binding protein            | 1.092   | 0.758  |
| DespoDRAFT_03133 | SH3 domain protein   | 1.258   | 0.431  |
| DespoDRAFT_03134 | outer membrane protein   | 1.184   | 0.675  |
| DespoDRAFT_03135 | hypothetical protein   | 1.768   | 0.0834 |
| DespoDRAFT_03136 | uncharacterized protein possibly involved in aromatic compounds catabolism | 1.327   | 0.146  |
| DespoDRAFT_03137 | shikimate kinase   | #VALUE! | 0.993  |
| DespoDRAFT_03138 | 3-phosphoshikimate 1-carboxyvinyltransferase                               | -1.083  | 0.319  |
| DespoDRAFT_03139 | shikimate 5-dehydrogenase  | 1.146   | 0.194  |
| DespoDRAFT_03140 | monofunctional chorismate mutase   | 1.39    | 0.119  |
| DespoDRAFT_03141 | phosphopantetheinyl transferase  | 1.316   | 0.775  |
| DespoDRAFT_03143 | putative polymerase with PALM domain HD hydrolase domain and Zn ribbon     | 1.477   | 0.125  |
| DespoDRAFT_03144 | (E)-4-hydroxy-3-methyl-but-2-enyl pyrophosphate reductase                  | 1.073   | 0.826  |
| DespoDRAFT_03145 | ParB-like partition protein  | 1.616   | 0.227  |
| DespoDRAFT_03146 | ATPase involved in chromosome partitioning                                 | 1.442   | 0.0364 |
| DespoDRAFT_03147 | ATP-dependent helicase HrpA  | -1.587  | 0.0709 |
| DespoDRAFT_03148 | YgiT-type zinc finger domain protein                                       | -2.593  | 0.0779 |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_03149 | hypothetical protein   | -2.524 | 0.141  |
| DespoDRAFT_03150 | hypothetical protein   | -3.706 | 0.0219 |
| DespoDRAFT_03153 | hypothetical protein   | -1.156 | 0.796  |
| DespoDRAFT_03154 | protein encoded in hypervariable junctions of pilus gene clusters  | -1.438 | 0.524  |
| DespoDRAFT_03156 | PEP-CTERM putative exosortase interaction domain-containing protein  | -1.544 | 0.336  |
| DespoDRAFT_03157 | hypothetical protein   | -1.397 | 0.672  |
| DespoDRAFT_03158 | peptidase T-like protein   | -1.169 | 0.389  |
| DespoDRAFT_03159 | TIGR00299 family protein   | 1.361  | 0.106  |
| DespoDRAFT_03160 | phosphatidylglycerophosphatase A-like protein  | 1.341  | 0.426  |
| DespoDRAFT_03161 | protein RecA   | 2.085  | 0.0995 |
| DespoDRAFT_03162 | alanine--tRNA ligase   | 1.895  | 0.14   |
| DespoDRAFT_03163 | ABC-type uncharacterized transport system permease component   | 3.041  | 0.0541 |
| DespoDRAFT_03164 | ABC-type uncharacterized transport system permease component   | 2.622  | 0.133  |
| DespoDRAFT_03166 | hypothetical protein   | 1.271  | 0.579  |
| DespoDRAFT_03167 | long-chain fatty acid transport protein  | 1.545  | 0.0995 |
| DespoDRAFT_03173 | glycosyltransferase  | 1.774  | 0.664  |
| DespoDRAFT_03174 | hypothetical protein   | -2.944 | NaN    |
| DespoDRAFT_03175 | RecA-superfamily ATPase possibly involved in signal transduction   | -1.618 | 0.073  |
| DespoDRAFT_03176 | KaiB domain-containing protein   | -1.506 | 0.57   |
| DespoDRAFT_03177 | PAS domain S-box   | -2.217 | 0.0881 |
| DespoDRAFT_03178 | histidine kinase Response regulator receiver domain protein histidine kinase GAF domain-containing protein | -1.983 | 0.0869 |
| DespoDRAFT_03179 | arsenite efflux pump ACR3-like permease  | -2.33  | 0.0164 |
| DespoDRAFT_03180 | methylase of chemotaxis methyl-accepting protein   | 1.487  | 0.432  |
| DespoDRAFT_03181 | chemotaxis response regulator containing a CheY-like receiver domain and a methylesterase domain           | 1.271  | 0.248  |
| DespoDRAFT_03182 | chemotaxis protein histidine kinase-like protein   | 1.625  | 0.182  |
| DespoDRAFT_03183 | PAS domain S-box   | 1.488  | 0.285  |
| DespoDRAFT_03184 | methyl-accepting chemotaxis protein  | 2.224  | 0.0698 |
| DespoDRAFT_03185 | chemotaxis signal transduction protein   | 2.793  | 0.116  |
| DespoDRAFT_03186 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains                         | 1.036  | 0.867  |
| DespoDRAFT_03187 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding                                 | -1.32  | 0.536  |

|                  | domains  |         |         |
|------------------|--|---------|---------|
| DespoDRAFT_03188 | hypothetical protein   | -1.572  | 0.373   |
| DespoDRAFT_03189 | CoA-substrate-specific enzyme activase putative                                | -1.839  | 0.182   |
| DespoDRAFT_03190 | Benzoyl-CoA reductase/2-hydroxyglutaryl-CoA dehydratase subunit BcrC/BadD/HgdB | -1.473  | 0.0403  |
| DespoDRAFT_03191 | Fe-S oxidoreductase  | 2.456   | 0.0595  |
| DespoDRAFT_03192 | hypothetical protein   | 1.085   | 0.242   |
| DespoDRAFT_03193 | hypothetical protein   | 1.59    | 0.147   |
| DespoDRAFT_03194 | hypothetical protein   | -1.413  | 0.45    |
| DespoDRAFT_03195 | DNA/RNA helicase superfamily II SNF2 family                                    | -1.405  | 0.188   |
| DespoDRAFT_03196 | hypothetical protein   | -1.31   | 0.357   |
| DespoDRAFT_03197 | PAS domain S-box   | 1.055   | 0.935   |
| DespoDRAFT_03198 | hypothetical protein   | -1.545  | 0.437   |
| DespoDRAFT_03199 | D-alanyl-D-alanine carboxypeptidase  | -1.032  | 0.741   |
| DespoDRAFT_03200 | transcriptional accessory protein  | 1.19    | 0.477   |
| DespoDRAFT_03201 | chaperonin GroL  | -1.83   | 0.083   |
| DespoDRAFT_03202 | acetyltransferase  | 1.895   | 0.714   |
| DespoDRAFT_03203 | ATP-grasp enzyme D-alanine-D-alanine ligase                                    | 1.059   | 0.958   |
| DespoDRAFT_03204 | ATP-grasp enzyme D-alanine-D-alanine ligase                                    | 1.73    | 0.421   |
| DespoDRAFT_03205 | KamA family protein  | 1.11    | 0.917   |
| DespoDRAFT_03206 | ATP-dependent protease La  | -1.009  | 0.986   |
| DespoDRAFT_03207 | ATPase involved in chromosome partitioning                                     | -11.654 | 0.00258 |
| DespoDRAFT_03209 | molecular chaperone (small heat shock protein)                                 | -5.738  | 0.0463  |
| DespoDRAFT_03210 | 1, 4-alpha-glucan branching enzyme   | -7.425  | 0.0342  |
| DespoDRAFT_03211 | hypothetical protein   | 1.045   | NaN     |
| DespoDRAFT_03217 | hypothetical protein   | -1.161  | 0.915   |
| DespoDRAFT_03218 | hypothetical protein   | -1.292  | 0.846   |
| DespoDRAFT_03219 | hypothetical protein   | -2.487  | 0.381   |
| DespoDRAFT_03220 | hypothetical protein   | -1.842  | 0.309   |
| DespoDRAFT_03221 | hypothetical protein   | -1.668  | 0.525   |
| DespoDRAFT_03222 | hypothetical protein   | -1.827  | 0.518   |
| DespoDRAFT_03223 | hypothetical protein   | -1.87   | 0.592   |
| DespoDRAFT_03224 | putative endonuclease containing a URI domain                                  | -1.776  | 0.347   |
| DespoDRAFT_03225 | hypothetical protein   | -1.192  | 0.886   |
| DespoDRAFT_03226 | site-specific recombinase DNA invertase Pin                                    | -2.556  | 0.119   |
| DespoDRAFT_03227 | hypothetical protein   | -1.762  | 0.189   |

|                  |  |         |         |
|------------------|--|---------|---------|
| DespoDRAFT_03228 | hypothetical protein                                       | 1.222   | NaN     |
| DespoDRAFT_03229 | hypothetical protein                                       | -1.635  | NaN     |
| DespoDRAFT_03230 | hypothetical protein                                       | -3.126  | NaN     |
| DespoDRAFT_03231 | PAS domain S-box   | -2.513  | 0.148   |
| DespoDRAFT_03232 | hypothetical protein                                       | -3.805  | 0.107   |
| DespoDRAFT_03233 | molecular chaperone (small heat shock protein)             | -24.987 | 0.135   |
| DespoDRAFT_03234 | PAS domain-containing protein                              | -8.047  | 0.0569  |
| DespoDRAFT_03235 | hypothetical protein                                       | -2.453  | NaN     |
| DespoDRAFT_03236 | hypothetical protein                                       | -14.984 | 0.0674  |
| DespoDRAFT_03238 | putative regulatory protein FmdB family                    | -3.088  | 0.0413  |
| DespoDRAFT_03239 | hypothetical protein                                       | -1.75   | 0.12    |
| DespoDRAFT_03240 | D-alanine aminotransferase                                 | -2.44   | 0.12    |
| DespoDRAFT_03241 | uncharacterized protein involved in cysteine biosynthesis  | -1.081  | 0.842   |
| DespoDRAFT_03242 | hypothetical protein                                       | -1.707  | 0.282   |
| DespoDRAFT_03243 | hypothetical protein                                       | 1.635   | 0.349   |
| DespoDRAFT_03244 | polyferredoxin heterodixulfide reductase subunit A         | 1.863   | 0.0192  |
| DespoDRAFT_03245 | coenzyme F420-reducing hydrogenase delta subunit           | 2.325   | 0.068   |
| DespoDRAFT_03246 | Methylene-tetrahydrofolate reductase                       | 1.803   | 0.00623 |
| DespoDRAFT_03247 | 5, 10-methylenetetrahydrofolate reductase                  | 2.077   | 0.0387  |
| DespoDRAFT_03248 | iron-sulfur cluster biosynthesis protein NifU-like protein | 1.37    | 0.577   |
| DespoDRAFT_03249 | hypothetical protein                                       | -2.366  | 0.0477  |
| DespoDRAFT_03250 | Zn-dependent hydrolase glyoxylase                          | -1.598  | 0.152   |
| DespoDRAFT_03251 | S-adenosylmethionine decarboxylase proenzyme               | 2.212   | 0.21    |
| DespoDRAFT_03252 | spermidine synthase  | 4.295   | 0.0805  |
| DespoDRAFT_03253 | acetyltransferase  | -1.238  | 0.0992  |
| DespoDRAFT_03254 | hypothetical protein                                       | -1.089  | 0.545   |
| DespoDRAFT_03255 | cell wall-associated hydrolase invasion-associated protein | -1.523  | 0.297   |
| DespoDRAFT_03256 | flagellar basal body rod protein                           | -1.938  | 0.233   |
| DespoDRAFT_03257 | SprA-related family  | -1.939  | 0.109   |
| DespoDRAFT_03258 | imidazoleglycerol-phosphate dehydratase                    | 1.046   | 0.902   |
| DespoDRAFT_03259 | DNA primase catalytic core                                 | 1.103   | 0.142   |
| DespoDRAFT_03260 | RNA polymerase sigma factor sigma-70 family                | 1.624   | 0.0447  |
| DespoDRAFT_03262 | dinuclear metal center protein YbgI/SA1388 family          | 1.747   | 0.375   |
| DespoDRAFT_03263 | Zn-ribbon protein  | 1.249   | 0.497   |
| DespoDRAFT_03265 | HPr-related phosphotransferase system component            | -1.251  | 0.426   |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_03266 | 2-C-methyl-D-erythritol 4-phosphate cytidyltransferase                             | 1.136  | 0.808  |
| DespoDRAFT_03267 | ABC-type nitrate/sulfonate/bicarbonate transport system periplasmic component      | -3.835 | 0.0437 |
| DespoDRAFT_03268 | hypothetical protein   | -1.174 | 0.663  |
| DespoDRAFT_03269 | putative Ser protein kinase  | -2.361 | 0.0523 |
| DespoDRAFT_03270 | hypothetical protein   | -2.829 | 0.08   |
| DespoDRAFT_03271 | hypothetical protein   | -2.31  | 0.229  |
| DespoDRAFT_03272 | putative Ser protein kinase  | -2.114 | 0.0613 |
| DespoDRAFT_03273 | response regulator containing a CheY-like receiver domain and an HD-GYP domain     | -1.705 | 0.11   |
| DespoDRAFT_03274 | single-stranded-DNA-specific exonuclease RecJ                                      | 1.953  | 0.286  |
| DespoDRAFT_03275 | hypothetical protein   | -1.709 | 0.312  |
| DespoDRAFT_03276 | tRNA-N(6)-(isopentenyl)adenosine-37 thiotransferase enzyme MiaB                    | 1.236  | 0.0574 |
| DespoDRAFT_03277 | methionine aminopeptidase type I   | -1.101 | 0.771  |
| DespoDRAFT_03278 | 1-acyl-sn-glycerol-3-phosphate acyltransferase                                     | 2.055  | 0.149  |
| DespoDRAFT_03279 | nitrogenase iron protein   | -3.079 | 0.0244 |
| DespoDRAFT_03280 | nifD nitrogenase molybdenum-iron protein alpha chain                               | -1.681 | 0.262  |
| DespoDRAFT_03281 | nifK nitrogenase molybdenum-iron protein beta chain                                | 2.291  | 0.653  |
| DespoDRAFT_03282 | nifE nitrogenase MoFe cofactor biosynthesis protein NifE                           | -1.039 | 0.964  |
| DespoDRAFT_03283 | nifK2 Nitrogenase molybdenum-iron protein  | -1.002 | 0.998  |
| DespoDRAFT_03284 | nifB nitrogenase cofactor biosynthesis protein NifB                                | -1.56  | 0.696  |
| DespoDRAFT_03285 | ferredoxin   | 1.096  | NaN    |
| DespoDRAFT_03286 | isopropylmalate/homocitrate/citramalate synthase                                   | -5.555 | 0.176  |
| DespoDRAFT_03287 | PEP-CTERM putative exosortase interaction domain-containing protein                | -2.68  | 0.105  |
| DespoDRAFT_03288 | uncharacterized protein MTH1187 family   | 1.018  | 0.628  |
| DespoDRAFT_03289 | ATP dependent DNA ligase-like protein  | -2.111 | 0.0636 |
| DespoDRAFT_03290 | ribulose-5-phosphate 4-epimerase-like epimerase or aldolase                        | -2.584 | 0.0556 |
| DespoDRAFT_03291 | response regulator with CheY-like receiver AAA-type ATPase and DNA-binding domains | -5.7   | 0.225  |
| DespoDRAFT_03292 | signal transduction histidine kinase   | -3.047 | 0.0636 |
| DespoDRAFT_03294 | ABC-type cobalt transport system permease component CbiQ                           | 1.686  | 0.79   |
| DespoDRAFT_03295 | ABC-type cobalt transport system ATPase  | 1.127  | 0.286  |

|                  | component  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_03296 | hypothetical protein   | -1.122 | 0.847  |
| DespoDRAFT_03297 | birA biotin-(acetyl-CoA-carboxylase) ligase                                | 1.821  | 0.349  |
| DespoDRAFT_03298 | putative Rossmann fold nucleotide-binding protein                          | -1.072 | 0.216  |
| DespoDRAFT_03299 | hypothetical protein   | -1.292 | 0.205  |
| DespoDRAFT_03300 | glycogen/starch/alpha-glucan phosphorylase                                 | -1.423 | 0.0893 |
| DespoDRAFT_03301 | dTDP-glucose 4 6-dehydratase   | -2.057 | 0.066  |
| DespoDRAFT_03302 | Protein of unknown function (DUF1703)                                      | -2.582 | 0.0261 |
| DespoDRAFT_03303 | protein of unknown function (DUF1902)                                      | -2.731 | 0.111  |
| DespoDRAFT_03304 | putative exonuclease of the beta-lactamase fold involved in RNA processing | -2.553 | 0.0675 |
| DespoDRAFT_03305 | hypothetical protein   | -2.083 | 0.414  |
| DespoDRAFT_03306 | PIN domain-containing protein  | -2.089 | 0.227  |
| DespoDRAFT_03307 | putative nucleotidyltransferase  | -2.051 | 0.231  |
| DespoDRAFT_03308 | hypothetical protein   | -2.43  | 0.104  |
| DespoDRAFT_03309 | YgiT-type zinc finger domain protein                                       | -1.906 | 0.0606 |
| DespoDRAFT_03310 | restriction endonuclease   | -1.6   | 0.0964 |
| DespoDRAFT_03311 | addiction module antidote protein HigA family                              | -1.847 | 0.259  |
| DespoDRAFT_03312 | plasmid maintenance system killer protein                                  | -2.194 | 0.0362 |
| DespoDRAFT_03314 | hypothetical protein   | 1.34   | 0.228  |
| DespoDRAFT_03317 | Protein of unknown function (DUF2281)                                      | -1.918 | 0.0522 |
| DespoDRAFT_03318 | growth inhibitor   | -1.972 | 0.135  |
| DespoDRAFT_03319 | addiction module antidote protein HigA family                              | -2.03  | 0.18   |
| DespoDRAFT_03320 | putative nucleotidyltransferase  | 1.028  | 0.954  |
| DespoDRAFT_03321 | hypothetical protein   | -1.706 | 0.0913 |
| DespoDRAFT_03322 | hypothetical protein   | -2.167 | 0.143  |
| DespoDRAFT_03324 | hypothetical protein   | -1.89  | 0.373  |
| DespoDRAFT_03325 | hypothetical protein   | -2.34  | 0.116  |
| DespoDRAFT_03326 | hypothetical protein   | -2.856 | 0.182  |
| DespoDRAFT_03327 | hypothetical protein   | -2.395 | 0.13   |
| DespoDRAFT_03328 | putative kinase galactokinase/mevalonate kinase                            | -1.815 | 0.12   |
| DespoDRAFT_03329 | glucose-1-phosphate cytidyltransferase                                     | -1.704 | 0.132  |
| DespoDRAFT_03330 | nucleoside-diphosphate-sugar epimerase                                     | -2.193 | 0.0676 |
| DespoDRAFT_03331 | dTDP-4-dehydrorhamnose 3, 5-epimerase                                      | -2.646 | 0.0704 |
| DespoDRAFT_03332 | NAD dependent epimerase/dehydratase family protein                         | -1.59  | 0.145  |
| DespoDRAFT_03333 | nucleoside-diphosphate-sugar epimerase                                     | -2.004 | 0.0345 |
| DespoDRAFT_03335 | Na+-driven multidrug efflux pump   | -4.475 | 0.0111 |
| DespoDRAFT_03336 | hypothetical protein   | -1.584 | 0.432  |

|                  |  |         |        |
|------------------|--|---------|--------|
| DespoDRAFT_03337 | hypothetical protein   | -2.326  | 0.0604 |
| DespoDRAFT_03339 | Na <sup>+</sup> -driven multidrug efflux pump                        | -2.856  | 0.125  |
| DespoDRAFT_03341 | hypothetical protein   | #VALUE! | NaN    |
| DespoDRAFT_03342 | glycosyltransferase  | -2.095  | 0.177  |
| DespoDRAFT_03343 | hypothetical protein   | -2.985  | 0.149  |
| DespoDRAFT_03345 | coenzyme F390 synthetase   | -1.288  | 0.249  |
| DespoDRAFT_03346 | hypothetical protein   | -1.124  | 0.661  |
| DespoDRAFT_03347 | glycosyltransferase  | -1.746  | 0.237  |
| DespoDRAFT_03348 | Heparinase II/III-like protein                                       | -1.499  | 0.281  |
| DespoDRAFT_03349 | nucleotide sugar dehydrogenase                                       | -1.681  | 0.086  |
| DespoDRAFT_03351 | glycosyltransferase  | -2.866  | 0.0437 |
| DespoDRAFT_03353 | hypothetical protein   | -1.415  | 0.473  |
| DespoDRAFT_03354 | putative nucleic acid-binding protein                                | -1.399  | 0.103  |
| DespoDRAFT_03355 | hypothetical protein   | -2.299  | 0.182  |
| DespoDRAFT_03357 | hypothetical protein   | -2.418  | 0.332  |
| DespoDRAFT_03358 | transposase  | -2.419  | 0.0805 |
| DespoDRAFT_03359 | exopolysaccharide biosynthesis polyprenyl glycosylphosphotransferase | -2.112  | 0.109  |
| DespoDRAFT_03360 | hypothetical protein   | -3.475  | 0.0806 |
| DespoDRAFT_03362 | PilZ domain-containing protein                                       | 1.565   | 0.335  |
| DespoDRAFT_03363 | hypothetical protein   | -2.058  | 0.0635 |
| DespoDRAFT_03364 | hypothetical protein   | -1.148  | 0.436  |
| DespoDRAFT_03365 | periplasmic protein involved in polysaccharide export                | -1.411  | 0.112  |
| DespoDRAFT_03366 | uncharacterized protein involved in exopolysaccharide biosynthesis   | -1.557  | 0.157  |
| DespoDRAFT_03367 | lipid A core-O-antigen ligase-like enzyme                            | -1.155  | 0.254  |
| DespoDRAFT_03368 | hypothetical protein   | -1.116  | 0.603  |
| DespoDRAFT_03369 | hypothetical protein   | -1.085  | 0.711  |
| DespoDRAFT_03370 | hypothetical protein   | -1.733  | 0.235  |
| DespoDRAFT_03371 | hypothetical protein   | -1.019  | 0.977  |
| DespoDRAFT_03372 | FAD-dependent dehydrogenase  | -1.097  | 0.877  |
| DespoDRAFT_03373 | putative pyridoxal-dependent aspartate 1-decarboxylase               | 1.871   | 0.128  |
| DespoDRAFT_03374 | hypothetical protein   | -2.584  | 0.409  |
| DespoDRAFT_03375 | ribosomal subunit interface protein                                  | -2.147  | 0.379  |
| DespoDRAFT_03376 | arginine kinase  | -1.615  | 0.386  |
| DespoDRAFT_03377 | hypothetical protein   | 1.45    | 0.468  |
| DespoDRAFT_03378 | MoxR-like ATPase   | 1.405   | 0.0248 |
| DespoDRAFT_03379 | hypothetical protein   | 1.225   | 0.16   |
| DespoDRAFT_03380 | hypothetical protein   | 1.225   | 0.41   |
| DespoDRAFT_03381 | Mg-chelatase subunit ChlD  | -1.096  | 0.772  |
| DespoDRAFT_03382 | von Willebrand factor type A-like protein                            | 1.08    | 0.828  |
| DespoDRAFT_03383 | tetratricopeptide repeat protein                                     | -2.188  | 0.0728 |
| DespoDRAFT_03384 | glycerol-3-phosphate dehydrogenase                                   | 2.704   | 0.199  |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_03385 | putative signal transduction protein   | 1.783  | 0.104  |
| DespoDRAFT_03386 | ribonuclease HI  | 1.218  | 0.143  |
| DespoDRAFT_03387 | hypothetical protein   | -2.085 | 0.086  |
| DespoDRAFT_03388 | ABC-type transport system involved in resistance to organic solvents auxiliary component | -2.6   | 0.0193 |
| DespoDRAFT_03389 | phosphate ABC transporter permease protein PstC  | -1.212 | 0.768  |
| DespoDRAFT_03390 | phosphate ABC transporter permease protein PstA  | 1.149  | 0.779  |
| DespoDRAFT_03391 | ABC-type phosphate transport system periplasmic component                                | -1.291 | 0.434  |
| DespoDRAFT_03392 | phosphate ABC transporter ATP-binding protein  | 1.036  | 0.954  |
| DespoDRAFT_03393 | hypothetical protein   | 1.083  | 0.711  |
| DespoDRAFT_03394 | exodeoxyribonuclease III   | 1.017  | 0.931  |
| DespoDRAFT_03395 | ferredoxin-thioredoxin reductase catalytic subunit                                       | -1.314 | 0.0952 |
| DespoDRAFT_03396 | glutaredoxin-like protein  | -1.438 | 0.166  |
| DespoDRAFT_03397 | hypothetical protein   | -1.676 | 0.0728 |
| DespoDRAFT_03398 | desulfoferredoxin  | -2.048 | 0.0493 |
| DespoDRAFT_03399 | TIGR01777 family protein   | -1.737 | 0.102  |
| DespoDRAFT_03400 | hypothetical protein   | -1.217 | 0.59   |
| DespoDRAFT_03401 | exopolyphosphatase-like enzyme   | -1.552 | 0.086  |
| DespoDRAFT_03402 | rubredoxin   | -1.873 | 0.0706 |
| DespoDRAFT_03403 | cytochrome d oxidase cyd subunit II  | -1.088 | 0.733  |
| DespoDRAFT_03404 | cytochrome bd-type quinol oxidase subunit 1  | -1.651 | 0.0134 |
| DespoDRAFT_03405 | Protein of unknown function DUF255   | 2.587  | 0.261  |
| DespoDRAFT_03406 | 5"-deoxy-5"-methylthioadenosine phosphorylase  | 1.878  | 0.108  |
| DespoDRAFT_03407 | adenine phosphoribosyltransferase  | 1.555  | 0.193  |
| DespoDRAFT_03408 | hypothetical protein   | 1.542  | 0.324  |
| DespoDRAFT_03409 | exodeoxyribonuclease V gamma subunit   | 1.096  | 0.597  |
| DespoDRAFT_03410 | exodeoxyribonuclease V beta subunit  | -1.244 | 0.133  |
| DespoDRAFT_03411 | putative membrane protein  | -1.785 | 0.0709 |
| DespoDRAFT_03412 | protein of unknown function (DUF2760)  | 1.336  | 0.127  |
| DespoDRAFT_03413 | molecular chaperone  | 1.447  | 0.0827 |
| DespoDRAFT_03414 | molecular chaperone  | 1.112  | 0.456  |
| DespoDRAFT_03415 | hypothetical protein   | -1.221 | 0.395  |
| DespoDRAFT_03418 | hypothetical protein   | 1.027  | 0.951  |
| DespoDRAFT_03419 | putative membrane protein  | 1.586  | 0.596  |
| DespoDRAFT_03420 | Rhodanese-related sulfurtransferase  | 1.037  | 0.413  |
| DespoDRAFT_03421 | hypothetical protein   | 2.825  | 0.0335 |
| DespoDRAFT_03422 | hypothetical protein   | -1.018 | 0.922  |



|                  |   |        |         |
|------------------|---|--------|---------|
| DespoDRAFT_03423 | L-threonine 3-dehydrogenase   | -2.125 | 0.0224  |
| DespoDRAFT_03424 | 7-keto-8-aminopelargonate synthetase-like enzyme                              | -2.251 | 0.186   |
| DespoDRAFT_03425 | hypothetical protein  | -1.852 | 0.0753  |
| DespoDRAFT_03426 | hypothetical protein  | 2.46   | 0.111   |
| DespoDRAFT_03427 | hypothetical protein  | -2.189 | 0.188   |
| DespoDRAFT_03428 | diguanylate cyclase (GGDEF) domain-containing protein                         | -1.297 | 0.185   |
| DespoDRAFT_03429 | hypothetical protein  | -2.215 | 0.0328  |
| DespoDRAFT_03430 | ABC-type nitrate/sulfonate/bicarbonate transport system periplasmic component | -1.882 | 0.0336  |
| DespoDRAFT_03431 | ABC-type nitrate/sulfonate/bicarbonate transport system permease component    | -1.669 | 0.253   |
| DespoDRAFT_03432 | ABC-type nitrate/sulfonate/bicarbonate transport system periplasmic component | 1.156  | 0.773   |
| DespoDRAFT_03433 | ABC-type nitrate/sulfonate/bicarbonate transport system ATPase component      | -2.915 | 0.29    |
| DespoDRAFT_03434 | ABC-type nitrate/sulfonate/bicarbonate transport system periplasmic component | -2.599 | 0.135   |
| DespoDRAFT_03435 | putative unusual protein kinase   | -1.812 | 0.1     |
| DespoDRAFT_03436 | hypothetical protein  | -1.559 | 0.103   |
| DespoDRAFT_03437 | acyl-CoA dehydrogenase  | 1.233  | 0.0826  |
| DespoDRAFT_03438 | metal-dependent hydrolase beta-lactamase superfamily I                        | -1.364 | 0.443   |
| DespoDRAFT_03439 | Major Facilitator Superfamily transporter                                     | -1.381 | 0.737   |
| DespoDRAFT_03440 | hypothetical protein  | 2.369  | 0.285   |
| DespoDRAFT_03441 | hypothetical protein  | -1.838 | 0.644   |
| DespoDRAFT_03442 | putative transcriptional regulator  | -1.584 | 0.397   |
| DespoDRAFT_03443 | HipA domain-containing protein  | -1.329 | 0.0952  |
| DespoDRAFT_03444 | Rhodopirellula transposase  | 2.454  | 0.16    |
| DespoDRAFT_03445 | Rhodopirellula transposase  | 1.007  | 0.96    |
| DespoDRAFT_03446 | hypothetical protein  | 1.017  | 0.886   |
| DespoDRAFT_03447 | Zn-dependent oxidoreductase NADPH:quinone reductase                           | -1.408 | 0.16    |
| DespoDRAFT_03449 | ADP-ribosylglycohydrolase   | -2.705 | 0.00432 |
| DespoDRAFT_03450 | putative transcriptional regulator  | -2.075 | 0.0409  |
| DespoDRAFT_03451 | deoxyribodipyrimidine photolyase  | -2.098 | 0.0935  |
| DespoDRAFT_03452 | methylase involved in ubiquinone/menaquinone biosynthesis                     | -2.278 | 0.0841  |
| DespoDRAFT_03453 | methylase involved in ubiquinone/menaquinone biosynthesis                     | -1.627 | 0.0381  |
| DespoDRAFT_03454 | putative transcription activator  | -3.937 | 0.0145  |
| DespoDRAFT_03455 | hypothetical protein  | -1.589 | 0.503   |
| DespoDRAFT_03456 | transposase   | -1.021 | 0.968   |
| DespoDRAFT_03457 | hypothetical protein  | -1.003 | 0.998   |

|                  |   |        |        |
|------------------|---|--------|--------|
| DespoDRAFT_03458 | Acetate permease  | -1.004 | 0.993  |
| DespoDRAFT_03459 | hypothetical protein  | -1.334 | 0.783  |
| DespoDRAFT_03462 | glycosyltransferase   | -1.071 | 0.488  |
| DespoDRAFT_03463 | dTDP-4-dehydrothamnose 3, 5-epimerase-like enzyme               | -2.109 | 0.534  |
| DespoDRAFT_03466 | putative glycosyltransferase                                    | -2.551 | 0.108  |
| DespoDRAFT_03467 | hypothetical protein  | -1.594 | 0.138  |
| DespoDRAFT_03468 | DnaJ-class molecular chaperone with C-terminal Zn finger domain | -1.206 | 0.273  |
| DespoDRAFT_03469 | dihydrodipicolinate reductase                                   | 1.741  | 0.0949 |
| DespoDRAFT_03470 | Nucleoside-diphosphate-sugar pyrophosphorylase family protein   | 2.053  | 0.263  |
| DespoDRAFT_03471 | glycerol-3-phosphate O-acyltransferase                          | 1.15   | 0.402  |
| DespoDRAFT_03472 | hypothetical protein  | 1.278  | 0.611  |
| DespoDRAFT_03473 | hypothetical protein  | -1.692 | 0.0734 |
| DespoDRAFT_03474 | histidinol-phosphate aminotransferase                           | 3.642  | 0.159  |
| DespoDRAFT_03475 | cytidylate kinase   | 3.502  | 0.0282 |
| DespoDRAFT_03476 | ribosomal protein S1  | 2.468  | 0.0423 |
| DespoDRAFT_03477 | signal peptide peptidase SppA, 36K type                         | 1.012  | 0.847  |
| DespoDRAFT_03478 | Sua5/YciO/YrdC/YwIC family protein                              | 1.842  | 0.0614 |
| DespoDRAFT_03479 | 6-phosphofructokinase   | 2.074  | 0.0557 |
| DespoDRAFT_03480 | inosine-5"-monophosphate dehydrogenase                          | 1.465  | 0.249  |
| DespoDRAFT_03481 | DNA-directed DNA polymerase III PolC                            | 1.295  | 0.0575 |
| DespoDRAFT_03482 | putative periplasmic or secreted lipoprotein                    | 1.34   | 0.309  |
| DespoDRAFT_03483 | hypothetical protein  | -2.078 | 0.143  |
| DespoDRAFT_03484 | protein with DnaJ-like domain                                   | 1.366  | 0.269  |
| DespoDRAFT_03485 | hypothetical protein  | -1.078 | 0.884  |
| DespoDRAFT_03486 | valyl-tRNA synthetase   | -1.064 | 0.531  |
| DespoDRAFT_03487 | nicotinate-nucleotide pyrophosphorylase                         | 1.006  | 0.99   |
| DespoDRAFT_03488 | hypothetical protein  | 1.139  | 0.802  |
| DespoDRAFT_03489 | hypothetical protein  | -3.126 | NaN    |
| DespoDRAFT_03490 | hypothetical protein  | -1.605 | 0.273  |
| DespoDRAFT_03492 | hypothetical protein  | -1.933 | 0.12   |
| DespoDRAFT_03493 | diguanylate cyclase (GGDEF) domain-containing protein           | -1.306 | 0.411  |
| DespoDRAFT_03494 | GTP-binding protein LepA  | 1.013  | 0.853  |
| DespoDRAFT_03495 | 2-isopropylmalate synthase/homocitrate synthase family protein  | 2.786  | 0.0565 |
| DespoDRAFT_03496 | acetolactate synthase small subunit                             | 3.656  | 0.0162 |
| DespoDRAFT_03497 | acetolactate synthase large subunit biosynthetic type           | 2.923  | 0.0438 |
| DespoDRAFT_03498 | dihydroxy-acid dehydratase                                      | 1.329  | 0.0737 |
| DespoDRAFT_03499 | hypothetical protein  | -1.827 | 0.112  |
| DespoDRAFT_03501 | hypothetical protein  | 1.354  | 0.763  |
| DespoDRAFT_03502 | NCAIR mutase-like protein                                       | 1.438  | 0.18   |

|                  |   |        |        |
|------------------|---|--------|--------|
| DespoDRAFT_03504 | histidine kinase  | -1.081 | 0.898  |
| DespoDRAFT_03505 | response regulator containing a CheY-like receiver domain and an HTH DNA-binding domain | 1.05   | 0.937  |
| DespoDRAFT_03506 | cytochrome c peroxidase   | -2.482 | 0.698  |
| DespoDRAFT_03507 | hypothetical protein  | -4.313 | 0.0311 |
| DespoDRAFT_03508 | methyltransferase putative  | 1.12   | 0.892  |
| DespoDRAFT_03509 | Protein of unknown function (DUF1698)   | -1.22  | 0.753  |
| DespoDRAFT_03510 | hypothetical protein  | -4.475 | 0.216  |
| DespoDRAFT_03511 | arginase  | -1.159 | 0.812  |
| DespoDRAFT_03512 | helicase family protein with metal-binding cysteine cluster                             | 1.022  | 0.88   |
| DespoDRAFT_03514 | exopolyphosphatase-like enzyme  | 1.096  | 0.143  |
| DespoDRAFT_03515 | hypothetical protein  | 1.527  | 0.158  |
| DespoDRAFT_03516 | dGTP triphosphohydrolase  | 1.829  | 0.166  |
| DespoDRAFT_03517 | ATPase involved in chromosome partitioning  | 1.153  | 0.284  |
| DespoDRAFT_03518 | hypothetical protein  | -1.652 | 0.111  |
| DespoDRAFT_03519 | tetratricopeptide repeat protein  | 1.087  | 0.816  |
| DespoDRAFT_03520 | DNA-directed RNA polymerase sigma subunit (sigma70/sigma32)                             | 1.064  | 0.616  |
| DespoDRAFT_03521 | phosphoribosylaminoimidazole-succinocarboxamide synthase                                | -1.045 | 0.835  |
| DespoDRAFT_03522 | putative transcriptional regulator  | 1.165  | 0.0837 |
| DespoDRAFT_03523 | hypothetical protein  | 1.433  | 0.35   |
| DespoDRAFT_03524 | translation elongation factor-like GTPase   | 1.851  | 0.085  |
| DespoDRAFT_03525 | hemolysin A   | 2.81   | 0.099  |
| DespoDRAFT_03526 | 1-deoxy-D-xylulose-5-phosphate synthase   | 1.801  | 0.0821 |
| DespoDRAFT_03527 | geranylgeranyl pyrophosphate synthase   | 1.328  | 0.532  |
| DespoDRAFT_03528 | exodeoxyribonuclease VII small subunit  | 1.714  | 0.24   |
| DespoDRAFT_03529 | exodeoxyribonuclease VII large subunit  | 1.302  | 0.36   |
| DespoDRAFT_03530 | sugar phosphate isomerase/epimerase   | -1.029 | 0.944  |
| DespoDRAFT_03531 | Rhodanese-related sulfurtransferase   | -1.791 | 0.191  |
| DespoDRAFT_03532 | pyridine nucleotide-disulfide oxidoreductase family protein                             | -1.892 | 0.0842 |
| DespoDRAFT_03533 | hypothetical protein  | -2.336 | 0.204  |
| DespoDRAFT_03534 | methylase involved in ubiquinone/menaquinone biosynthesis                               | -2.387 | 0.0983 |
| DespoDRAFT_03535 | hypothetical protein  | -1.501 | 0.271  |
| DespoDRAFT_03537 | signal transduction histidine kinase  | -2.11  | 0.147  |
| DespoDRAFT_03538 | esterase/lipase   | -2.277 | 0.0816 |
| DespoDRAFT_03539 | acyl-CoA dehydrogenase  | -1.38  | 0.0937 |
| DespoDRAFT_03540 | hypothetical protein  | 1.46   | 0.355  |
| DespoDRAFT_03541 | FRG domain protein  | 1.944  | 0.121  |
| DespoDRAFT_03542 | putative methyltransferase YaeB/AF_0241   | 1.155  | 0.676  |

|                  |   |        |        |
|------------------|---|--------|--------|
|                  | family  |        |        |
| DespoDRAFT_03543 | oligoendopeptidase F  | 1.048  | 0.71   |
| DespoDRAFT_03544 | gamma-glutamyl phosphate reductase  | 1.234  | 0.17   |
| DespoDRAFT_03545 | glutamate 5-kinase  | 2.354  | 0.0241 |
| DespoDRAFT_03547 | hypothetical protein  | -1.262 | 0.631  |
| DespoDRAFT_03548 | penicilin amidase   | -1.867 | 0.0414 |
| DespoDRAFT_03549 | phage shock protein C   | -1.878 | 0.128  |
| DespoDRAFT_03550 | hypothetical protein  | -1.778 | 0.149  |
| DespoDRAFT_03551 | phage shock protein A   | -2.3   | 0.0633 |
| DespoDRAFT_03552 | psp operon transcriptional activator PspF                                   | -2.225 | 0.0111 |
| DespoDRAFT_03553 | LysM repeat-containing protein  | -1.735 | 0.461  |
| DespoDRAFT_03554 | YeeE/YedE family protein (DUF395)   | 1.327  | 0.184  |
| DespoDRAFT_03555 | putative redox protein regulator of disulfide bond formation                | 1.183  | 0.134  |
| DespoDRAFT_03556 | Protein of unknown function (DUF3343)                                       | 1.011  | 0.937  |
| DespoDRAFT_03557 | putative sugar kinase   | 1.109  | 0.501  |
| DespoDRAFT_03558 | hypothetical protein  | 1.223  | 0.746  |
| DespoDRAFT_03559 | L-asparaginase/GlutRNAGln amidotransferase subunit D                        | 1.174  | 0.646  |
| DespoDRAFT_03560 | protein-tyrosine-phosphatase  | 1.735  | 0.272  |
| DespoDRAFT_03561 | isochorismate synthase  | 1.526  | 0.344  |
| DespoDRAFT_03562 | ATPase involved in chromosome partitioning                                  | -1.2   | 0.585  |
| DespoDRAFT_03563 | hypothetical protein  | 1.135  | 0.894  |
| DespoDRAFT_03564 | hypothetical protein  | -1.051 | 0.866  |
| DespoDRAFT_03565 | AIPR protein  | -1.405 | 0.277  |
| DespoDRAFT_03566 | Transposase IS66 family   | -5.497 | 0.108  |
| DespoDRAFT_03567 | Protein of unknown function (DUF3089)                                       | -5.044 | 0.0487 |
| DespoDRAFT_03568 | hypothetical protein  | -1.62  | 0.467  |
| DespoDRAFT_03569 | putative peptidoglycan-binding domain-containing protein                    | -1.716 | 0.162  |
| DespoDRAFT_03570 | hypothetical protein  | -1.478 | 0.276  |
| DespoDRAFT_03571 | 2-succinyl-5-enolpyruvyl-6-hydroxy-3-cyclohexene-1-carboxylic-acid synthase | -1.834 | 0.0831 |
| DespoDRAFT_03572 | dihydroxynaphthoate synthase  | -1.409 | 0.354  |
| DespoDRAFT_03573 | enolase superfamily enzyme related to L-alanine-DL-glutamate epimerase      | -1.737 | 0.116  |
| DespoDRAFT_03574 | acyl-CoA synthetase (AMP-forming)/AMP-acid ligase II                        | -2.081 | 0.225  |
| DespoDRAFT_03575 | hypothetical protein  | -1.147 | 0.345  |
| DespoDRAFT_03576 | indolepyruvate ferredoxin oxidoreductase alpha subunit                      | -1.114 | 0.534  |
| DespoDRAFT_03577 | 2-oxoacid:ferredoxin oxidoreductase gamma subunit                           | -1.017 | 0.964  |
| DespoDRAFT_03578 | 3-dehydroquininate dehydratase type II                                      | -1.314 | 0.227  |

|                  |  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_03579 | Mg-dependent DNase   | -1.169 | 0.309  |
| DespoDRAFT_03580 | dinucleotide-utilizing enzyme possibly involved in molybdopterin or thiamin biosynthesis | -1.206 | 0.644  |
| DespoDRAFT_03581 | hypothetical protein   | 2.321  | 0.331  |
| DespoDRAFT_03586 | hypothetical protein   | -1.563 | NaN    |
| DespoDRAFT_03587 | hypothetical protein   | 1.833  | NaN    |
| DespoDRAFT_03589 | hypothetical protein   | -2.382 | 0.445  |
| DespoDRAFT_03593 | addiction module antidote protein HigA family  | -4.674 | 0.325  |
| DespoDRAFT_03594 | hypothetical protein   | -2.49  | 0.131  |
| DespoDRAFT_03595 | transcriptional regulator  | 2.07   | 0.29   |
| DespoDRAFT_03596 | tryptophan synthase beta subunit   | 3.606  | 0.0403 |
| DespoDRAFT_03597 | tryptophan synthase alpha subunit  | 2.794  | 0.137  |
| DespoDRAFT_03598 | S-methyl-5-thioribose-1-phosphate isomerase  | 1.24   | 0.651  |
| DespoDRAFT_03599 | transcriptional regulator  | 1.563  | 0.41   |
| DespoDRAFT_03600 | Fe-S oxidoreductase  | -1.063 | 0.906  |
| DespoDRAFT_03601 | hypothetical protein   | -1.198 | 0.653  |
| DespoDRAFT_03602 | ABC-type metal ion transport system periplasmic component/surface adhesin                | -1.729 | 0.23   |
| DespoDRAFT_03603 | ATPase component of Mn/Zn ABC-type transporter   | -1.137 | 0.0733 |
| DespoDRAFT_03604 | ABC-type Mn <sup>2+</sup> /Zn <sup>2+</sup> transport system permease component          | -1.748 | 0.0264 |
| DespoDRAFT_03605 | urocanate hydratase  | -1.897 | 0.0753 |
| DespoDRAFT_03606 | acyl-CoA synthetase (AMP-forming)/AMP-acid ligase II                                     | 1.484  | 0.58   |
| DespoDRAFT_03607 | Fe <sup>2+</sup> transport system protein A  | -1.426 | 0.161  |
| DespoDRAFT_03608 | ferrous iron transporter FeoB  | 1.884  | 0.144  |
| DespoDRAFT_03609 | hypothetical protein   | 1.906  | 0.301  |
| DespoDRAFT_03610 | methylase involved in ubiquinone/menaquinone biosynthesis                                | 1.102  | 0.843  |
| DespoDRAFT_03611 | 3-hydroxyacyl-CoA dehydrogenase  | -1.387 | 0.0128 |
| DespoDRAFT_03612 | acetyl-CoA acetyltransferase   | -1.627 | 0.158  |
| DespoDRAFT_03613 | universal stress protein UspA-like protein   | -1.685 | 0.0338 |
| DespoDRAFT_03614 | signal transduction histidine kinase   | -5.631 | 0.0708 |
| DespoDRAFT_03615 | hypothetical protein   | -3.129 | 0.506  |
| DespoDRAFT_03616 | hypothetical protein   | -1.085 | 0.854  |
| DespoDRAFT_03617 | hypothetical protein   | -1.284 | 0.253  |
| DespoDRAFT_03623 | hypothetical protein   | 1.436  | NaN    |
| DespoDRAFT_03624 | hypothetical protein   | -1.139 | 0.846  |
| DespoDRAFT_03625 | hydroxyethylthiazole kinase sugar kinase family  | -1.467 | 0.582  |
| DespoDRAFT_03628 | Protein of unknown function DUF55  | -1.415 | 0.886  |

|                  |   |         |        |
|------------------|---|---------|--------|
| DespoDRAFT_03630 | uncharacterized protein MTH1187 family  | -1.694  | 0.158  |
| DespoDRAFT_03631 | thiamine monophosphate synthase   | -1.746  | 0.167  |
| DespoDRAFT_03632 | protein of unknown function (DUF364)  | -1.583  | 0.254  |
| DespoDRAFT_03633 | thioredoxin   | -1.606  | 0.19   |
| DespoDRAFT_03635 | signal transduction histidine kinase<br>nitrate/nitrite-specific                                  | -1.625  | 0.449  |
| DespoDRAFT_03636 | uncharacterized protein, possibly involved<br>in aromatic compounds catabolism                    | 2.548   | 0.276  |
| DespoDRAFT_03637 | phosphoribosylformimino-5-<br>aminoimidazole carboxamide ribotide<br>isomerase eukaryotic type    | 1.133   | 0.748  |
| DespoDRAFT_03638 | ABC-type uncharacterized transport system<br>auxiliary component                                  | 3.527   | 0.419  |
| DespoDRAFT_03639 | ABC-type transport system involved in<br>resistance to organic solvents, periplasmic<br>component | 1.56    | 0.0333 |
| DespoDRAFT_03640 | ABC-type transport system involved in<br>resistance to organic solvents ATPase<br>component       | -1.051  | 0.756  |
| DespoDRAFT_03641 | putative integral membrane protein  | 1.213   | 0.448  |
| DespoDRAFT_03642 | purine nucleoside phosphorylase   | -1.958  | 0.425  |
| DespoDRAFT_03643 | putative membrane protein   | -1.634  | 0.472  |
| DespoDRAFT_03644 | ribosomal protein L11 methyltransferase   | 1.264   | 0.355  |
| DespoDRAFT_03645 | signal transduction histidine kinase  | -1.282  | 0.504  |
| DespoDRAFT_03646 | response regulator containing a CheY-like<br>receiver domain and an HTH DNA-binding<br>domain     | -1.627  | 0.0684 |
| DespoDRAFT_03647 | acyl-CoA synthetase (AMP-forming)/AMP-<br>acid ligase II  | -1.13   | 0.674  |
| DespoDRAFT_03648 | hydroxyethylthiazole kinase sugar kinase<br>family  | -1.05   | 0.847  |
| DespoDRAFT_03649 | Mn <sup>2+</sup> /Fe <sup>2+</sup> transporter NRAMP family                                       | 1.26    | 0.664  |
| DespoDRAFT_03650 | protein chain release factor B  | -1.102  | 0.716  |
| DespoDRAFT_03651 | hypothetical protein  | 1.139   | 0.931  |
| DespoDRAFT_03652 | RND family efflux transporter   | -1.729  | 0.0307 |
| DespoDRAFT_03653 | ABC-type antimicrobial peptide transport<br>system ATPase component                               | -2.284  | 0.203  |
| DespoDRAFT_03654 | ABC-type transport system involved in<br>lipoprotein release permease component                   | -1.995  | 0.515  |
| DespoDRAFT_03655 | ABC-type transport system involved in<br>lipoprotein release permease component                   | -1.932  | 0.648  |
| DespoDRAFT_03656 | phosphatidylserine decarboxylase  | 3.025   | NaN    |
| DespoDRAFT_03657 | Prolipoprotein diacylglyceryl transferase   | 1.34    | 0.878  |
| DespoDRAFT_03658 | hypothetical protein  | #VALUE! | NaN    |
| DespoDRAFT_03659 | acyl-CoA thioesterase II  | -1.907  | 0.489  |

|                  |  |          |         |
|------------------|--|----------|---------|
| DespoDRAFT_03660 | periplasmic component of amino acid ABC-type transporter/signal transduction system                              | 1.125    | 0.783   |
| DespoDRAFT_03661 | small-conductance mechanosensitive channel   | 1.787    | 0.0803  |
| DespoDRAFT_03663 | dihydroorotate dehydrogenase   | -1.595   | 0.0291  |
| DespoDRAFT_03664 | hypothetical protein   | 1.011    | 0.924   |
| DespoDRAFT_03665 | hypothetical protein   | 1.087    | 0.629   |
| DespoDRAFT_03666 | hypothetical protein   | 1.436    | 0.206   |
| DespoDRAFT_03667 | hypothetical protein   | -1.388   | 0.122   |
| DespoDRAFT_03669 | TIGR01777 family protein   | -1.742   | 0.0448  |
| DespoDRAFT_03670 | hypothetical protein   | -1.107   | 0.176   |
| DespoDRAFT_03671 | Zn-dependent hydrolase glyoxylase  | -1.41    | 0.18    |
| DespoDRAFT_03673 | cysteine desulfurase NifS  | -1.71    | 0.0858  |
| DespoDRAFT_03674 | Fe-S cluster assembly protein NifU   | -2.342   | 0.0467  |
| DespoDRAFT_03675 | TIGR02757 family protein   | -1.521   | 0.128   |
| DespoDRAFT_03676 | K <sup>+</sup> -dependent Na <sup>+</sup> exchanger related-protein  | -1.008   | 0.993   |
| DespoDRAFT_03677 | hypothetical protein   | -1.069   | 0.936   |
| DespoDRAFT_03678 | pyrroline-5-carboxylate reductase (proC)   | -1.914   | 0.0723  |
| DespoDRAFT_03679 | hypothetical protein   | -3.559   | 0.0413  |
| DespoDRAFT_03680 | rubredoxin   | -3.538   | 0.0509  |
| DespoDRAFT_03681 | chorismate synthase  | -1.702   | 0.227   |
| DespoDRAFT_03682 | sigma-54 interacting regulator   | -1.043   | 0.956   |
| DespoDRAFT_03683 | beta-ketoacyl synthase family protein<br>acyltransferase family protein<br>phosphopantetheine-containing protein | 1.824    | 0.0332  |
| DespoDRAFT_03684 | phosphopantetheinyl transferase  | 1.378    | 0.0958  |
| DespoDRAFT_03685 | response regulator with CheY-like receiver<br>AAA-type ATPase and DNA-binding<br>domains                         | -16.288  | 0.0337  |
| DespoDRAFT_03686 | tetratricopeptide repeat protein   | -18.462  | 0.0383  |
| DespoDRAFT_03687 | hypothetical protein   | -43.147  | 0.104   |
| DespoDRAFT_03688 | putative Fe-S oxidoreductase   | -49.794  | 0.0463  |
| DespoDRAFT_03689 | hypothetical protein   | -84.061  | 0.0731  |
| DespoDRAFT_03690 | hypothetical protein   | -53.439  | 0.0902  |
| DespoDRAFT_03691 | Ig-like domain-containing surface protein  | -41.827  | 0.0875  |
| DespoDRAFT_03692 | Phage tail protein   | -83.573  | 0.0963  |
| DespoDRAFT_03693 | Baseplate J-like protein   | -71.037  | 0.159   |
| DespoDRAFT_03694 | Baseplate J-like protein   | -71.463  | 0.0826  |
| DespoDRAFT_03695 | phage baseplate assembly protein W   | -90.216  | 0.0733  |
| DespoDRAFT_03696 | hypothetical protein   | -59.868  | 0.0467  |
| DespoDRAFT_03698 | phage protein D  | -43.42   | 0.0408  |
| DespoDRAFT_03699 | hypothetical protein   | -79.847  | 0.119   |
| DespoDRAFT_03700 | hypothetical protein   | -99.796  | 0.108   |
| DespoDRAFT_03701 | hypothetical protein   | -108.093 | 0.00853 |
| DespoDRAFT_03702 | AAA+ family ATPase   | -92.893  | 0.0863  |

|                  |   |          |         |
|------------------|---|----------|---------|
| DespoDRAFT_03703 | hypothetical protein  | -112.027 | 0.0964  |
| DespoDRAFT_03704 | putative phage tail region protein                                  | -157.538 | 0.0265  |
| DespoDRAFT_03705 | phage tail sheath protein FI  | -97.677  | 0.0543  |
| DespoDRAFT_03706 | hypothetical protein  | -186.056 | 0.00262 |
| DespoDRAFT_03707 | hypothetical protein  | -98.865  | 0.0586  |
| DespoDRAFT_03708 | putative phage tail region protein                                  | -92.353  | 0.00136 |
| DespoDRAFT_03709 | phage tail sheath protein FI  | -95.675  | 0.0254  |
| DespoDRAFT_03710 | phage tail sheath protein FI  | -66.537  | 0.00802 |
| DespoDRAFT_03711 | hypothetical protein  | -65.612  | 0.0561  |
| DespoDRAFT_03712 | hypothetical protein  | -52.23   | 0.0433  |
| DespoDRAFT_03713 | hypothetical protein  | -80.282  | 0.0397  |
| DespoDRAFT_03714 | cAMP-binding protein  | -2.089   | 0.398   |
| DespoDRAFT_03715 | hypothetical protein  | 1.835    | 0.679   |
| DespoDRAFT_03716 | peptidyl-prolyl cis-trans isomerase (rotamase) - cyclophilin family | 1.295    | 0.0851  |
| DespoDRAFT_03717 | monofunctional biosynthetic peptidoglycan transglycosylase          | -1.315   | 0.186   |
| DespoDRAFT_03718 | hypothetical protein  | 1.954    | 0.227   |
| DespoDRAFT_03719 | phosphohistidine phosphatase SixA                                   | -1.481   | 0.327   |
| DespoDRAFT_03720 | hypothetical protein  | 1.955    | 0.138   |
| DespoDRAFT_03721 | peroxiredoxin   | -1.317   | 0.229   |
| DespoDRAFT_03722 | universal stress protein UspA-like protein                          | -1.643   | 0.186   |
| DespoDRAFT_03723 | hypothetical protein  | -1.306   | 0.155   |
| DespoDRAFT_03725 | hypothetical protein  | -2.217   | 0.134   |
| DespoDRAFT_03727 | transposase   | -1.678   | 0.298   |
| DespoDRAFT_03728 | hypothetical protein  | -1.145   | 0.272   |
| DespoDRAFT_03729 | hypothetical protein  | -1.305   | 0.225   |
| DespoDRAFT_03730 | hypothetical protein  | -1.801   | 0.106   |
| DespoDRAFT_03731 | transposase   | -2.052   | 0.0452  |
| DespoDRAFT_03732 | transposase   | -1.449   | 0.262   |
| DespoDRAFT_03734 | prevent-host-death family protein                                   | 1.42     | 0.268   |
| DespoDRAFT_03736 | hypothetical protein  | -1.489   | 0.292   |
| DespoDRAFT_03737 | VRR-NUC domain-containing protein                                   | 1.758    | 0.24    |
| DespoDRAFT_03738 | hypothetical protein  | -1.021   | 0.971   |
| DespoDRAFT_03739 | hypothetical protein  | -1.434   | 0.0952  |
| DespoDRAFT_03740 | putative transcriptional regulator                                  | -2.482   | 0.157   |
| DespoDRAFT_03741 | hypothetical protein  | 2.895    | 0.5     |
| DespoDRAFT_03743 | hypothetical protein  | -1.544   | 0.628   |
| DespoDRAFT_03744 | hypothetical protein  | -1.396   | NaN     |
| DespoDRAFT_03745 | hypothetical protein  | -1.908   | 0.662   |
| DespoDRAFT_03746 | hypothetical protein  | 1.582    | 0.61    |
| DespoDRAFT_03747 | hypothetical protein  | -1.177   | 0.273   |
| DespoDRAFT_03748 | hypothetical protein  | -1.765   | 0.111   |
| DespoDRAFT_03749 | hypothetical protein  | -3.931   | 0.158   |
| DespoDRAFT_03750 | site-specific recombinase DNA invertase                             | -3.003   | 0.0958  |



|                  | Pin  |        |        |
|------------------|--|--------|--------|
| DespoDRAFT_03751 | hypothetical protein   | -5.274 | 0.186  |
| DespoDRAFT_03752 | hypothetical protein   | -2.172 | 0.258  |
| DespoDRAFT_03753 | hypothetical protein   | -1.771 | 0.188  |
| DespoDRAFT_03754 | site-specific recombinase DNA invertase<br>Pin   | -2.162 | 0.0965 |
| DespoDRAFT_03755 | NAD(P)H-nitrite reductase  | 1.046  | 0.103  |
| DespoDRAFT_03756 | prephenate dehydrogenase   | -1.159 | 0.445  |
| DespoDRAFT_03757 | response regulator with CheY-like receiver<br>AAA-type ATPase and DNA-binding<br>domains | -1.497 | 0.267  |
| DespoDRAFT_03758 | signal transduction histidine kinase   | -1.108 | 0.744  |
| DespoDRAFT_03759 | hypothetical protein   | -3.866 | 0.036  |
| DespoDRAFT_03760 | 2-keto-4-pentenoate hydratase/2-oxohepta-<br>3-ene-1, 7-dioic acid hydratase             | -1.212 | 0.199  |
| DespoDRAFT_03761 | hypothetical protein   | -1.065 | 0.959  |
| DespoDRAFT_03762 | trypsin-like serine protease with C-terminal<br>PDZ domain                               | -1.8   | 0.443  |
| DespoDRAFT_03763 | thiamine biosynthesis protein ThiF family 2  | -1.994 | 0.0681 |
| DespoDRAFT_03764 | thiazole biosynthesis protein ThiH   | -2.995 | 0.0888 |
| DespoDRAFT_03765 | putative enzyme of thiazole biosynthesis   | -2.01  | 0.0982 |
| DespoDRAFT_03766 | thiamine biosynthesis protein ThiS   | -2.079 | 0.0601 |
| DespoDRAFT_03767 | diaminopimelate epimerase  | 1.249  | 0.691  |
| DespoDRAFT_03768 | ribonuclease D   | 2.151  | 0.141  |
| DespoDRAFT_03769 | threonyl-tRNA synthetase   | 1.609  | 0.0835 |
| DespoDRAFT_03770 | metal-dependent hydrolase beta-lactamase<br>superfamily II                               | 1.152  | 0.447  |
| DespoDRAFT_03771 | Mg/Co/Ni transporter MgtE with CBS<br>domain   | -1.261 | 0.176  |
| DespoDRAFT_03772 | universal stress protein UspA-like protein   | -1.204 | 0.214  |
| DespoDRAFT_03773 | hypothetical protein   | -1.997 | 0.253  |

## BIBLIOGRAPHY

1. **Lovley DR, Ueki T, Zhang T, Malvankar NS, Shrestha PM, Flanagan KA, Aklujkar M, Butler JE, Giloteaux L, Rotaru AE, Holmes DE, Franks AE, Orellana R, Risso C, Nevin KP.** 2011. *Geobacter*: the microbe electric's physiology, ecology, and practical applications. *Adv Microb Physiol* **59**:1-100.
2. **Williams KH, Bargar JR, Lloyd JR, Lovley DR.** 2012. Bioremediation of uranium-contaminated groundwater: a systems approach to subsurface biogeochemistry. *Curr Opin Biotech* **24**:1-9.
3. **Orellana R, Leavitt JJ, Comolli LR, Csencsits R, Janot N, Flanagan KA, Gray AS, Leang C, Izallalen M, Mester T, Lovley DR.** 2013. U(VI) Reduction by a Diversity of Outer Surface C-Type Cytochromes of *Geobacter sulfurreducens*. *Appl Environ Microbiol*.
4. **Wall JD, Krumholz LR.** 2006. Uranium reduction. *Annu Rev Microbiol* **60**:149-166.
5. **Bradford GR, Bakhtar D, Westcot D.** 1990. Uranium, Vanadium, and Molybdenum in Saline Waters of California. *J. Environ. Qual.* **19**:105-108.
6. **Shelobolina ES, Sullivan SA, O'Neill KR, Nevin KP, Lovley DR.** 2004. Isolation, Characterization, and U(VI)-Reducing Potential of a Facultatively Anaerobic, Acid-Resistant Bacterium from Low-pH, Nitrate- and U(VI)-Contaminated Subsurface Sediment and Description of *Salmonella subterranea* sp. nov. *Appl Environ Microb* **70**:2959-2965.
7. **Anderson RT, Vrionis HA, Ortiz-Bernad I, Resch CT, Long PE, Dayvault R, Karp K, Marutzky S, Metzler DR, Peacock A, White DC, Lowe M, Lovley DR.** 2003. Stimulating the in situ activity of *Geobacter* species to remove uranium from the groundwater of a uranium-contaminated aquifer. *Appl Environ Microb* **69**:5884-5891.
8. **Konhauser K.** 2007. Introduction to geomicrobiology. Blackwell Pub., Malden, MA.
9. **Lawrence Berkeley National Laboratory USDoEOoB, Environmental Research N, Accelerated Bioremediation Research P.** 1999. Bioremediation of metals and radionuclides : what it is and how ti works. [Lawrence Berkeley National Laboratory], [Berkeley, CA].
10. **Watanabe ME.** 2001. Can bioremediation bounce back? *Nat Biotech* **19**:1111-1115.
11. **Beyenal H, Sani RK, Peyton BM, Dohnalkova AC, Amonette JE, Lewandowski Z.** 2004. Uranium Immobilization by Sulfate-Reducing Biofilms. *Environ Sci Technol* **38**:2067-2074.
12. **Finneran KT, Anderson RT, Nevin KP, Lovley DR.** 2002. Potential for Bioremediation of Uranium-Contaminated Aquifers with Microbial U(VI) Reduction. *Soil and Sediment Contamination: An International Journal* **11**:339-357.
13. **Vishnivetskaya TA, Brandt CC, Madden AS, Drake MM, Kostka JE, Akob DM, Küsel K, Palumbo AV.** 2010. Microbial Community Changes in Response to Ethanol or Methanol Amendments for U(VI) Reduction. *Appl Environ Microb* **76**:5728-5735.

14. **Zhuang K, Ma E, Lovley DR, Mahadevan R.** 2012. The design of long-term effective uranium bioremediation strategy using a community metabolic model. *Biotechnology and Bioengineering* **109**:2475-2483.
15. **Francis A.** 2008. Microbial transformations of uranium in wastes and implication on its mobility, p. 713-722. *In* Merkel B, Hasche-Berger A (ed.), *Uranium, Mining and Hydrogeology*. Springer Berlin Heidelberg.
16. **Keith-Roach MJ, Livens FR.** 2002. Interactions of microorganisms with radionuclides. Elsevier, Amsterdam ; New York.
17. **Bargar JR, Bernier-Latmani R, Giammar DE, Tebo BM.** 2008. Biogenic Uraninite Nanoparticles and Their Importance for Uranium Remediation. *Elements* **4**:407-412.
18. **Lovley DR.** 2003. Cleaning up with genomics: Applying molecular biology to bioremediation. *Nat Rev Microbiol* **1**:35-44.
19. **Wilkins MJ, Livens FR, Vaughan DJ, Lloyd JR.** 2006. The impact of Fe(III)-reducing bacteria on uranium mobility. *Biogeochemistry* **78**:125-150.
20. **Lovley DR, Phillips EJP, Gorby YA, Landa ER.** 1991. Microbial Reduction of Uranium. *Nature* **350**:413-416.
21. **Tebo BM, Obraztsova AY.** 1998. Sulfate-reducing bacterium grows with Cr(VI), U(VI), Mn(IV), and Fe(III) as electron acceptors. *Fems Microbiol Lett* **162**:193-198.
22. **Sanford RA, Wu Q, Sung Y, Thomas SH, Amos BK, Prince EK, Löffler FE.** 2007. Hexavalent uranium supports growth of *Anaeromyxobacter dehalogenans* and *Geobacter* spp. with lower than predicted biomass yields. *Environmental Microbiology* **9**:2885-2893.
23. **Khijniak TV, Slobodkin AI, Coker V, Renshaw JC, Livens FR, Bonch-Osmolovskaya EA, Birkeland NK, Medvedeva-Lyalikova NN, Lloyd JR.** 2005. Reduction of uranium(VI) phosphate during growth of the thermophilic bacterium *Thermoterrabacterium ferrireducens*. *Appl Environ Microb* **71**:6423-6426.
24. **Francis AJ, Dodge CJ, Lu F, Halada GP, Clayton CR.** 1994. XPS and XANES Studies of Uranium Reduction by *Clostridium* sp. *Environ Sci Technol* **28**:636-639.
25. **Lovley DR, Phillips EJP.** 1992. Reduction of Uranium by *Desulfovibrio desulfuricans*. *Appl Environ Microb* **58**:850-856.
26. **Lovley DR, Roden EE, Phillips EJP, Woodward JC.** 1993. Enzymatic Iron and Uranium Reduction by Sulfate-Reducing Bacteria. *Mar Geol* **113**:41-53.
27. **Barton LL, Choudhury K, Thomson BM, Steenhoudt K, Groffman AR.** 1996. Bacterial reduction of soluble uranium: The first step of in situ immobilization of uranium. *Radioact Waste Manag* **20**:141-151.
28. **Payne RB, Gentry DA, Rapp-Giles BJ, Casalot L, Wall JD.** 2002. Uranium reduction by *Desulfovibrio desulfuricans* strain G20 and a cytochrome c3 mutant. *Appl Environ Microb* **68**:3129-3132.
29. **Lovley DR, Holmes DE, Nevin KP.** 2004. Dissimilatory Fe(III) and Mn(IV) reduction. *Adv Microb Physiol* **49**:219-286.
30. **Holmes DE, O'Neil RA, Vrionis HA, N'Guessan LA, Ortiz-Bernad I, Larrahondo MJ, Adams LA, Ward JA, Nicoll JS, Nevin KP, Chavan MA,**

- Johnson JP, Long PE, Lovley DR.** 2007. Subsurface clade of Geobacteraceae that predominates in a diversity of Fe(III)-reducing subsurface environments. *ISME J* **1**:663-677.
31. **Snoeyenbos-West OL, Nevin KP, Anderson RT, Lovley DR.** 2000. Enrichment of Geobacter Species in Response to Stimulation of Fe(III) Reduction in Sandy Aquifer Sediments. *Microb Ecol* **39**:153-167.
32. **Coppi MV, Leang C, Sandler SJ, Lovley DR.** 2001. Development of a genetic system for *Geobacter sulfurreducens*. *Appl Environ Microb* **67**:3180-3187.
33. **Methe BA, Webster J, Nevin K, Butler J, Lovley DR.** 2005. DNA microarray analysis of nitrogen fixation and Fe(III) reduction in *Geobacter sulfurreducens*. *Appl Environ Microb* **71**:2530-2538.
34. **Aklujkar M, Coppi MV, Leang C, Kim B-C, Chavan MA, Perpetua LA, Giloteaux L, Liu A, Holmes D.** 2013. Proteins involved in electron transfer to Fe(III) and Mn(IV) oxides by *Geobacter sulfurreducens* and *Geobacter uraniireducens*. *Microbiology*.
35. **Shrestha PM, Rotaru A-E, Summers ZM, Shrestha M, Liu F, Lovley DR.** 2013. Transcriptomic and genetic analysis of direct interspecies electron transfer. *Appl Environ Microb*.
36. **Rotaru A-E, Shrestha PM, Liu F, Ueki T, Nevin K, Summers ZM, Lovley DR.** 2012. Interspecies electron transfer via H<sub>2</sub> and formate rather than direct electrical connections in co-cultures of *Pelobacter carbinolicus* and *Geobacter sulfurreducens*. *Appl Environ Microb*.
37. **Strycharz SM, Glaven RH, Coppi MV, Gannon SM, Perpetua LA, Liu A, Nevin KP, Lovley DR.** 2011. Gene expression and deletion analysis of mechanisms for electron transfer from electrodes to *Geobacter sulfurreducens*. *Bioelectrochemistry* **80**:142-150.
38. **Qiu Y, Cho BK, Park YS, Lovley D, Palsson BO, Zengler K.** 2010. Structural and operational complexity of the *Geobacter sulfurreducens* genome. *Genome research* **20**:1304-1311.
39. **Krushkal J, Juarez K, Barbe JF, Qu Y, Andrade A, Puljic M, Adkins RM, Lovley DR, Ueki T.** 2010. Genome-wide survey for PilR recognition sites of the metal-reducing prokaryote *Geobacter sulfurreducens*. *Gene* **469**:31-44.
40. **Juárez K, Byoung-Chan K, Nevin K, Olvera L, Reguera G, Lovley DR, Methé BA.** 2009. PilR, a Transcriptional Regulator for Pilin and Other Genes Required for Fe(III) Reduction in *Geobacter sulfurreducens*. *Journal of Molecular Microbiology & Biotechnology* **16**:146-158.
41. **Leang C, Krushkal J, Ueki T, Puljic M, Sun J, Juarez K, Nunez C, Reguera G, DiDonato R, Postier B, Adkins RM, Lovley DR.** 2009. Genome-wide analysis of the RpoN regulon in *Geobacter sulfurreducens*. *Bmc Genomics* **10**.
42. **Ding YHR, Hixson KK, Aklujkar MA, Lipton MS, Smith RD, Lovley DR, Mester T.** 2008. Proteome of *Geobacter sulfurreducens* grown with Fe(III) oxide or Fe(III) citrate as the electron acceptor. *Bba-Proteins Proteom* **1784**:1935-1941.
43. **Mahadevan R, Yan B, Postier B, Nevin KP, Woodard TL, O'Neil R, Coppi MV, Methe BA, Krushkal J.** 2008. Characterizing regulation of metabolism in *Geobacter sulfurreducens* through genome-wide expression data and sequence analysis. *Omics* **12**:33-+.

44. **Izallalen M, Mahadevan R, Burgard A, Postier B, Didonato R, Sun J, Schilling CH, Lovley DR.** 2008. *Geobacter sulfurreducens* strain engineered for increased rates of respiration. *Metab Eng* **10**:267-275.
45. **Kim BC, Postier BL, DiDonato RJ, Chaudhuri SK, Nevin KP, Lovley DR.** 2008. Insights into genes involved in electricity generation in *Geobacter sulfurreducens* via whole genome microarray analysis of the OmcF-deficient mutant. *Bioelectrochemistry* **73**:70-75.
46. **Yan B, Lovley DR, Krushkal J.** 2007. Genome-wide similarity search for transcription factors and their binding sites in a metal-reducing prokaryote *Geobacter sulfurreducens*. *Biosystems* **90**:421-441.
47. **Krushkal J, Yan B, DiDonato L, Puljic M, Nevin K, Woodard T, Adkins R, Methé B, Lovley D.** 2007. Genome-wide expression profiling in *Geobacter sulfurreducens*: identification of Fur and RpoS transcription regulatory sites in a rel Gsu mutant. *Funct Integr Genomics* **7**:229-255.
48. **Holmes DE, Chaudhuri SK, Nevin KP, Mehta T, Methe BA, Liu A, Ward JE, Woodard TL, Webster J, Lovley DR.** 2006. Microarray and genetic analysis of electron transfer to electrodes in *Geobacter sulfurreducens*. *Environmental Microbiology* **8**:1805-1815.
49. **Ding YHR, Hixson KK, Giometti CS, Stanley A, Esteve-Nunez A, Khare T, Tollaksen SL, Zhu WH, Adkins JN, Lipton MS, Smith RD, Mester T, Lovley DR.** 2006. The proteome of dissimilatory metal-reducing microorganism *Geobacter sulfurreducens* under various growth conditions. *Bba-Proteins Proteom* **1764**:1198-1206.
50. **Nunez C, Esteve-Nunez A, Giometti C, Tollaksen S, Khare T, Lin W, Lovley DR, Methe BA.** 2006. DNA microarray and proteomic analyses of the RpoS regulon in *Geobacter sulfurreducens*. *J Bacteriol* **188**:2792-2800.
51. **Krushkal J, Puljic M, Bin Y, Barbe JF, Mahadevan R, Postier B, O'Neil RA, Reguera G, Ching L, DiDonato LN, Nunez C, Methe BA, Adkins RM, Lovley DR.** 2008. Genome Regions Involved in Multiple Regulatory Pathways Identified Using GSEL, A Genome-Wide Database of Regulatory Sequence Elements of *Geobacter sulfurreducens*, p. 424-431.
52. **Shelobolina ES, Coppi MV, Korenevsky AA, DiDonato LN, Sullivan SA, Konishi H, Xu HF, Leang C, Butler JE, Kim BC, Lovley DR.** 2007. Importance of c-type cytochromes for U(VI) reduction by *Geobacter sulfurreducens*. *BMC Microbiology* **7**:7-16.
53. **Lovley DR.** 1993. Dissimilatory metal reduction. *Annu Rev Microbiol* **47**:263-290.
54. **Lloyd JR, Leang C, Hodges Myerson AL, Coppi MV, Cuifo S, Methe B, Sandler SJ, Lovley DR.** 2003. Biochemical and genetic characterization of PpcA, a periplasmic c-type cytochrome in *Geobacter sulfurreducens*. *Biochem J* **369**:153-161.
55. **Marshall MJ, Beliaev AS, Dohnalkova AC, Kennedy DW, Shi L, Wang Z, Boyanov MI, Lai B, Kemner KM, McLean JS, Reed SB, Culley DE, Bailey VL, Simonson CJ, Saffarini DA, Romine MF, Zachara JM, Fredrickson JK.** 2006. c-Type Cytochrome-Dependent Formation of U(IV) Nanoparticles by *Shewanella oneidensis*. *PLoS Biol* **4**:e268.

56. **Payne RB, Casalot L, Rivere T, Terry JH, Larsen L, Giles BJ, Wall JD.** 2004. Interaction between uranium and the cytochrome c3 of *Desulfovibrio desulfuricans* strain G20. *Arch Microbiol* **181**:398-406.
57. **Wade Jr R, DiChristina TJ.** 2000. Isolation of U(VI) reduction-deficient mutants of *Shewanella putrefaciens*. *Fems Microbiol Lett* **184**:143-148.
58. **Reguera G, McCarthy KD, Mehta T, Nicoll JS, Tuominen MT, Lovley DR.** 2005. Extracellular electron transfer via microbial nanowires. *Nature* **435**:1098-1101.
59. **Malvankar NS, Vargas M, Nevin KP, Franks AE, Leang C, Kim BC, Inoue K, Mester T, Covalla SF, Johnson JP, Rotello VM, Tuominen MT, Lovley DR.** 2011. Tunable metallic-like conductivity in microbial nanowire networks. *Nature Nanotechnology* **6**:573-579.
60. **Cologgi DL, Lampa-Pastirk S, Speers AM, Kelly SD, Reguera G.** 2011. Extracellular reduction of uranium via *Geobacter* conductive pili as a protective cellular mechanism. *Proceedings of the National Academy of Sciences of the United States of America* **108**:15248-15252.
61. **Reguera G.** 2012. Electron transfer at the cell-uranium interface in *Geobacter* spp. *Biochemical Society transactions* **40**:1227-1232.
62. **Voordeckers JW, Kim BC, Izallalen M, Lovley DR.** 2010. Role of *Geobacter sulfurreducens* Outer Surface c-Type Cytochromes in Reduction of Soil Humic Acid and Anthraquinone-2,6-Disulfonate. *Appl Environ Microbiol* **76**:2371-2375.
63. **Gralnick JA, Newman DK.** 2007. Extracellular respiration. *Mol Microbiol* **65**:1-11.
64. **Lovley DR.** 2006. Bug juice: harvesting electricity with microorganisms. *Nat Rev Microbiol* **4**:497-508.
65. **Coppi MV, O'Neil RA, Leang C, Kaufmann F, Methe BA, Nevin KP, Woodard TL, Liu A, Lovley DR.** 2007. Involvement of *Geobacter sulfurreducens* SfrAB in acetate metabolism rather than intracellular, respiration-linked Fe(III) citrate reduction. *Microbiol-Sgm* **153**:3572-3585.
66. **Schnug E, Haneklaus S.** 2008. Dispersion of uranium in the environment by fertilization, p. 45-52. *In* Merkel B, Hasche-Berger A (ed.), *Uranium, Mining and Hydrogeology*. Springer Berlin Heidelberg.
67. **Hu P, Brodie EL, Suzuki Y, McAdams HH, Andersen GL.** 2005. Whole-genome transcriptional analysis of heavy metal stresses in *Caulobacter crescentus*. *J Bacteriol* **187**:8437-8449.
68. **Bencheikh-Latmani R, Williams SM, Haucke L, Criddle CS, Wu LY, Zhou JZ, Tebo BM.** 2005. Global transcriptional profiling of *Shewanella oneidensis* MR-1 during Cr(VI) and U(VI) reduction. *Appl Environ Microb* **71**:7453-7460.
69. **Nies DH, Silver S.** 1995. Ion Efflux Systems Involved in Bacterial Metal Resistances. *J Ind Microbiol* **14**:186-199.
70. **Canovas D, Cases I, de Lorenzo V.** 2003. Heavy metal tolerance and metal homeostasis in *Pseudomonas putida* as revealed by complete genome analysis. *Environmental Microbiology* **5**:1242-1256.
71. **Van Horn JD, Huang H.** 2006. Uranium(VI) bio-coordination chemistry from biochemical, solution and protein structural data. *Coordin Chem Rev* **250**:765-775.

72. **Nies DH.** 1999. Microbial heavy-metal resistance. *Appl Microbiol Biot* **51**:730-750.
73. **Snoeyenbos-West O, Van Praagh CG, Lovley DR.** 2001. *Trichlorobacter thiogenes* Should Be Renamed as a *Geobacter* Species. *Appl Environ Microb* **67**:1020-1022.
74. **Holmes DE, Finneran KT, O'Neil RA, Lovley DR.** 2002. Enrichment of Members of the Family *Geobacteraceae* Associated with Stimulation of Dissimilatory Metal Reduction in Uranium-Contaminated Aquifer Sediments. *Appl Environ Microb* **68**:2300-2306.
75. **Vrionis HA, Anderson RT, Ortiz-Bernad I, O'Neill KR, Resch CT, Peacock AD, Dayvault R, White DC, Long PE, Lovley DR.** 2005. Microbiological and Geochemical Heterogeneity in an In Situ Uranium Bioremediation Field Site. *Appl Environ Microb* **71**:6308-6318.
76. **Holmes DE, Nevin KP, O'Neil RA, Ward JE, Adams LA, Woodard TL, Vrionis HA, Lovley DR.** 2005. Potential for Quantifying Expression of the *Geobacteraceae* Citrate Synthase Gene To Assess the Activity of *Geobacteraceae* in the Subsurface and on Current-Harvesting Electrodes. *Appl Environ Microb* **71**:6870-6877.
77. **Ortiz-Bernad I, Anderson RT, Vrionis HA, Lovley DR.** 2004. Resistance of Solid-Phase U(VI) to Microbial Reduction during In Situ Bioremediation of Uranium-Contaminated Groundwater. *Appl Environ Microb* **70**:7558-7560.
78. **Miletto M, Williams KH, N'Guessan AL, Lovley DR.** 2011. Molecular Analysis of the Metabolic Rates of Discrete Subsurface Populations of Sulfate Reducers. *Appl Environ Microb* **77**:6502-6509.
79. **Chapelle FH, Lovley DR.** 1992. Competitive-Exclusion of Sulfate Reduction by Fe(II)-Reducing Bacteria - a Mechanism for Producing Discrete Zones of High-Iron Ground-Water. *Ground Water* **30**:29-36.
80. **Barlett M, Moon HS, Peacock AA, Hedrick DB, Williams KH, Long PE, Lovley D, Jaffe PR.** 2012. Uranium reduction and microbial community development in response to stimulation with different electron donors. *Biodegradation* **23**:535-546.
81. **Handley KM, VerBerkmoes NC, Steefel CI, Williams KH, Sharon I, Miller CS, Frischkorn KR, Chourey K, Thomas BC, Shah MB, Long PE, Hettich RL, Banfield JF.** 2013. Biostimulation induces syntrophic interactions that impact C, S and N cycling in a sediment microbial community. *Isme Journal* **7**:800-816.
82. **Handley KM, Wrighton KC, Piceno YM, Andersen GL, DeSantis TZ, Williams KH, Wilkins MJ, N'Guessan AL, Peacock A, Bargar J, Long PE, Banfield JF.** 2012. High-density PhyloChip profiling of stimulated aquifer microbial communities reveals a complex response to acetate amendment. *Fems Microbiol Ecol* **81**:188-204.
83. **Methé BA, Nelson KE, Eisen JA, Paulsen IT, Nelson W, Heidelberg JF, Wu D, Wu M, Ward N, Beanan MJ, Dodson RJ, Madupu R, Brinkac LM, Daugherty SC, DeBoy RT, Durkin AS, Gwinn M, Kolonay JF, Sullivan SA, Haft DH, Selengut J, Davidsen TM, Zafar N, White O, Tran B, Romero C, Forberger HA, Weidman J, Khouri H, Feldblyum TV, Utterback TR, Van**

- Aken SE, Lovley DR, Fraser CM.** 2003. Genome of *Geobacter sulfurreducens*: Metal Reduction in Subsurface Environments. *Science* **302**:1967-1969.
84. **Smith JA, Lovley DR, Tremblay P-L.** 2013. Outer Cell Surface Components Essential for Fe(III) Oxide Reduction by *Geobacter metallireducens*. *Appl Environ Microbiol* **79**:901-907.
85. **Summers ZM, Fogarty HE, Leang C, Franks AE, Malvankar NS, Lovley DR.** 2010. Direct Exchange of Electrons Within Aggregates of an Evolved Syntrophic Coculture of Anaerobic Bacteria. *Science* **330**:1413-1415.
86. **Reguera G, Nevin KP, Nicoll JS, Covalla SF, Woodard TL, Lovley DR.** 2006. Biofilm and Nanowire Production Leads to Increased Current in *Geobacter sulfurreducens* Fuel Cells. *Appl Environ Microbiol* **72**:7345-7348.
87. **Nevin KP, Kim BC, Glaven RH, Johnson JP, Woodard TL, Methe BA, DiDonato RJ, Covalla SF, Franks AE, Liu A, Lovley DR.** 2009. Anode Biofilm Transcriptomics Reveals Outer Surface Components Essential for High Density Current Production in *Geobacter sulfurreducens* Fuel Cells. *PLoS One* **4**:e5628.
88. **Vargas M, Malvankar NS, Tremblay P-L, Leang C, Smith JA, Patel P, Synoeyenbos-West O, Nevin KP, Lovley DR.** 2013. Aromatic Amino Acids Required for Pili Conductivity and Long-Range Extracellular Electron Transport in *Geobacter sulfurreducens*. *mBio* **4**:e00210-00213.
89. **Mehta T, Coppi MV, Childers SE, Lovley DR.** 2005. Outer membrane *c*-type cytochromes required for Fe(III) and Mn(IV) oxide reduction in *Geobacter sulfurreducens*. *Appl Environ Microbiol* **71**:8634-8641.
90. **Leang C, Qian XL, Mester T, Lovley DR.** 2010. Alignment of the *c*-Type Cytochrome OmcS along Pili of *Geobacter sulfurreducens*. *Appl Environ Microbiol* **76**:4080-4084.
91. **Lovley DR.** 2011. Live wires: direct extracellular electron exchange for bioenergy and the bioremediation of energy-related contamination. *Energ Environ Sci* **4**:4896-4906.
92. **Lovley DR.** 2012. Long-range electron transport to Fe(III) oxide via pili with metallic-like conductivity. *Biochem. Soc. Trans* **40**:1186-1190.
93. **Inoue K, Qian XL, Morgado L, Kim BC, Mester T, Izallalen M, Salgueiro CA, Lovley DR.** 2010. Purification and Characterization of OmcZ, an Outer-Surface, Octaheme *c*-Type Cytochrome Essential for Optimal Current Production by *Geobacter sulfurreducens*. *Appl Environ Microbiol* **76**:3999-4007.
94. **Inoue K, Leang C, Franks AE, Woodard TL, Nevin KP, Lovley DR.** 2011. Specific localization of the *c*-type cytochrome OmcZ at the anode surface in current-producing biofilms of *Geobacter sulfurreducens*. *Environmental Microbiology Reports* **3**:211-217.
95. **Qian XL, Reguera G, Mester T, Lovley DR.** 2007. Evidence that OmcB and OmpB of *Geobacter sulfurreducens* are outer membrane surface proteins. *Fems Microbiol Lett* **277**:21-27.
96. **Leang C, Coppi MV, Lovley DR.** 2003. OmcB, a *c*-type polyheme cytochrome, involved in Fe(III) reduction in *Geobacter sulfurreducens*. *J Bacteriol* **185**:2096-2103.



97. **Leang C, Adams LA, Chin KJ, Nevin KP, Methe BA, Webster J, Sharma ML, Lovley DR.** 2005. Adaptation to disruption of the electron transfer pathway for Fe(III) reduction in *Geobacter sulfurreducens*. *J Bacteriol* **187**:5918-5926.
98. **Qian XL, Mester T, Morgado L, Arakawa T, Sharma ML, Inoue K, Joseph C, Salgueiro CA, Maroney MJ, Lovley DR.** 2011. Biochemical characterization of purified OmcS, a *c*-type cytochrome required for insoluble Fe(III) reduction in *Geobacter sulfurreducens*. *Biochimica Et Biophysica Acta-Bioenergetics* **1807**:404-412.
99. **Lovley DR, Widman PK, Woodward JC, Phillips EJP.** 1993. Reduction of Uranium by Cytochrome *c*3 of *Desulfovibrio vulgaris*. *Appl Environ Microbiol* **59**:3572-3576.
100. **Comolli LR, Duarte R, Baum D, Luef B, Downing KH, Larson DM, Csencsits R, Banfield JF.** 2012. A portable cryo-plunger for on-site intact cryogenic microscopy sample preparation in natural environments. *Microsc Res Tech* **75**:829-836.
101. **Downing KH, Mooney PE.** 2008. A charge coupled device camera with electron decelerator for intermediate voltage electron microscopy. *Rev Sci Instrum* **79**:043702-043710
102. **Kremer JR, Mastronarde DN, McIntosh JR.** 1996. Computer visualization of three-dimensional image data using IMOD. *Journal of Structural Biology* **116**:71-76.
103. **Ravel B, Newville M.** 2005. Athena, Artemis, Hephaestus: Data Analysis for X-Ray Absorption Spectroscopy Using Ifeffit. *Journal of Synchrotron Radiation* **12**:537-541.
104. **Holmes DE, O'Neil RA, Chavan MA, N'Guessan LA, Vrionis HA, Perpetua LA, Larrahondo MJ, DiDonato R, Liu A, Lovley DR.** 2009. Transcriptome of *Geobacter uraniireducens* growing in uranium-contaminated subsurface sediments. *ISME J* **3**:216-230.
105. **Converse BJ, Wu T, Findlay RH, Roden EE.** 2013. U(VI) reduction in sulfate-reducing subsurface sediments amended with ethanol or acetate. *Appl Environ Microbiol* **79**:4173-4177.
106. **Newsome L, Morris K, Lloyd JR.** 2014. The biogeochemistry and bioremediation of uranium and other priority radionuclides. *Chemical Geology* **363**:164-184.
107. **Mahadevan R, Palsson BØ, Lovley DR.** 2011. *In situ* to *in silico* and back: elucidating the physiology and ecology of *Geobacter* spp. using genome-scale modelling. *Nat Rev Micro* **9**:39-50.
108. **Nies DH.** 2013. RND-efflux pumps for metal cations. Norwich: Horizon Scientific Press Ltd.
109. **Tran HT.** 2009. Investigation of chemotaxis genes and their functions in *Geobacter* species, p. xiii, 143 p. University of Massachusetts Amherst, Amherst, Mass.
110. **Caccavo F, Lonergan DJ, Lovley DR, Davis M, Stolz JF, Mcinerney MJ.** 1994. *Geobacter sulfurreducens* sp. nov., a Hydrogen-Oxidizing and Acetate-Oxidizing Dissimilatory Metal-Reducing Microorganism. *Appl Environ Microbiol* **60**:3752-3759.

111. **Eng JK, McCormack AL, Yates JR.** 1994. An Approach to Correlate Tandem Mass-Spectral Data of Peptides with Amino-Acid-Sequences in a Protein Database. *J Am Soc Mass Spectr* **5**:976-989.
112. **Mehta T, Childers SE, Glaven R, Lovley DR, Mester T.** 2006. A putative multicopper protein secreted by an atypical type II secretion system involved in the reduction of insoluble electron acceptors in *Geobacter sulfurreducens*. *Microbiology* **152**:2257-2264.
113. **Harkewicz R, Belov ME, Anderson GA, Pasa-Tolic L, Masselon CD, Prior DC, Udseth HR, Smith RD.** 2002. ESI-FTICR mass spectrometry employing data-dependent external ion selection and accumulation. *J Am Soc Mass Spectr* **13**:144-154.
114. **Lipton MS, Pasa-Tolic L, Anderson GA, Anderson DJ, Auberry DL, Battista KR, Daly MJ, Fredrickson J, Hixson KK, Kostandarithes H, Masselon C, Markillie LM, Moore RJ, Romine MF, Shen YF, Stritmatter E, Tolic N, Udseth HR, Venkateswaran A, Wong LK, Zhao R, Smith RD.** 2002. Global analysis of the *Deinococcus radiodurans* proteome by using accurate mass tags. *Proceedings of the National Academy of Sciences of the United States of America* **99**:11049-11054.
115. **Lovley DR, Phillips EJP.** 1988. Novel mode of microbial energy metabolism: organic carbon oxidation coupled to dissimilatory reduction of iron or manganese. *Appl Environ Microbiol* **54**:1472-1480.
116. **Yun J, Ueki T, Miletto M, Lovley DR.** 2011. Monitoring the Metabolic Status of *Geobacter* Species in Contaminated Groundwater by Quantifying Key Metabolic Proteins with *Geobacter*-Specific Antibodies. *Appl Environ Microbiol* **77**:4597-4602.
117. **Wilkins MJ, Callister SJ, Miletto M, Williams KH, Nicora CD, Lovley DR, Long PE, Lipton MS.** 2011. Development of a biomarker for *Geobacter* activity and strain composition; Proteogenomic analysis of the citrate synthase protein during bioremediation of U(VI). *Microb Biotechnol* **4**:55-63.
118. **Mahadevan R, Bond DR, Butler JE, Esteve-Nuñez A, Coppi MV, Palsson BO, Schilling CH, Lovley DR.** 2006. Characterization of Metabolism in the Fe(III)-Reducing Organism *Geobacter sulfurreducens* by Constraint-Based Modeling. *Appl Environ Microbiol* **72**:1558-1568.
119. **Maezato Y, Blum P.** 2012. Survival of the Fittest: Overcoming Oxidative Stress at the Extremes of Acid, Heat and Metal. *Life* **2**:229-242.
120. **Gray C.** 1994. Electron Microscopy of Protein-Nucleic Acid Complexes, p. 347-356. *In* Geoff Kneale G (ed.), *DNA-Protein Interactions*, vol. 30. Humana Press.
121. **Yazzie M, Gamble SL, Civitello ER, Stearns DM.** 2003. Uranyl acetate causes DNA single strand breaks in vitro in the presence of ascorbate (vitamin C). *Chem Res Toxicol* **16**:524-530.
122. **Mallika G, Barry R.** 2002. *Microbial Resistance Mechanisms for Heavy Metals and Metalloids*, *Heavy Metals In The Environment*. CRC Press.
123. **Zobel CR, Beer M.** 1961. Electron stains. I. Chemical studies on the interaction of DNA with uranyl salts. *J Biophys Biochem Cytol* **10**:335-346.
124. **Hartsock WJ, Cohen JD, Segal DJ.** 2007. Uranyl acetate as a direct inhibitor of DNA-binding proteins. *Chem Res Toxicol* **20**:784-789.

125. **Matsuda E, Nakajima A.** 2012. Effect of catechins and tannins on depleted uranium-induced DNA strand breaks. *Journal of Radioanalytical and Nuclear Chemistry* **293**:711-714.
126. **Kim EH, Nies DH, McEvoy MM, Rensing C.** 2011. Switch or Funnel: How RND-Type Transport Systems Control Periplasmic Metal Homeostasis. *J Bacteriol* **193**:2381-2387.
127. **Lloyd JR, Lovley DR.** 2001. Microbial detoxification of metals and radionuclides. *Curr Opin Biotech* **12**:248-253.
128. **Gadd GM.** 2010. Metals, minerals and microbes: geomicrobiology and bioremediation. *Microbiology* **156**:609-643.
129. **Merroun ML, Selenska-Pobell S.** 2008. Bacterial interactions with uranium: An environmental perspective. *J Contam Hydrol* **102**:285-295.
130. **Lin WC, Coppi MV, Lovley DR.** 2004. *Geobacter sulfurreducens* Can Grow with Oxygen as a Terminal Electron Acceptor. *Appl Environ Microbiol* **70**:2525-2528.
131. **Geslin C, Llanos J, Prieur D, Jeanthon C.** 2001. The manganese and iron superoxide dismutases protect *Escherichia coli* from heavy metal toxicity. *Res Microbiol* **152**:901-905.
132. **Privalle CT, Fridovich I.** 1987. Induction of Superoxide Dismutase in *Escherichia coli* by Heat Shock. *Proceedings of the National Academy of Sciences of the United States of America* **84**:2723-2726.
133. **Bernhardt J, Volker U, Volker A, Antelmann H, Schmid R, Mach H, Hecker M.** 1997. Specific and general stress proteins in *Bacillus subtilis* - A two-dimensional protein electrophoresis study. *Microbiology* **143**:999-1017.
134. **Chourey K, Thompson MR, Morrell-Falvey J, VerBerkmoes NC, Brown SD, Shah M, Zhou JZ, Doktycz M, Hettich RL, Thompson DK.** 2006. Global molecular and morphological effects of 24-hour chromium(VI) exposure on *Shewanella oneidensis* MR-1. *Appl Environ Microbiol* **72**:6331-6344.
135. **Roux M, Coves J.** 2002. The iron-containing superoxide dismutase of *Ralstonia metallidurans* CH34. *Fems Microbiol Lett* **210**:129-133.
136. **Pourahmad J, Ghashang M, Ettehadi HA, Ghalandari R.** 2006. A search for cellular and molecular mechanisms involved in depleted uranium (DU) toxicity. *Environmental Toxicology* **21**:349-354.
137. **Smirnova GV, Oktyabrsky ON.** 2005. Glutathione in Bacteria. *Biochemistry (Moscow)* **70**:1199-1211.
138. **Farr SB, Kogoma T.** 1991. Oxidative Stress Responses in *Escherichia coli* and *Salmonella typhimurium*. *Microbiol Rev* **55**:561-585.
139. **Mouser PJ, Holmes DE, Perpetua LA, DiDonato R, Postier B, Liu A, Lovley DR.** 2009. Quantifying expression of *Geobacter* spp. oxidative stress genes in pure culture and during *in situ* uranium bioremediation. *ISME J* **3**:454-465.
140. **Shelobolina ES, Vrionis HA, Findlay RH, Lovley DR.** 2008. *Geobacter uraniireducens* sp. nov., isolated from subsurface sediment undergoing uranium bioremediation. *International Journal of Systematic and Evolutionary Microbiology* **58**:1075-1078.
141. **Thauer RK, Mollerzinkhan D, Spormann AM.** 1989. Biochemistry of acetate catabolism in anaerobic chemotropic bacteria. *Annu Rev Microbiol* **43**:43-67.

142. **Mussmann M, Richter M, Lombardot T, Meyerdierks A, Kuever J, Kube M, Glöckner FO, Amann R.** 2005. Clustered Genes Related to Sulfate Respiration in Uncultured Prokaryotes Support the Theory of Their Concomitant Horizontal Transfer. *J Bacteriol* **187**:7126-7137.
143. **Muyzer G, Stams AJM.** 2008. The *ecology* and biotechnology of sulphate-reducing bacteria. *Nat Rev Micro* **6**:441-454.
144. **Hao OJ, Chen JM, Huang L, Buglass RL.** 1996. Sulfate reducing bacteria. *Critical Reviews in Environmental Science and Technology* **26**:155-187.
145. **Jorgensen BB.** 1982. Mineralization of Organic-Matter in the Sea Bed - the Role of Sulfate Reduction. *Nature* **296**:643-645.
146. **Chapelle FH, McMahon PB.** 1991. Geochemistry of Dissolved Inorganic Carbon in a Coastal-Plain Aquifer .1. Sulfate from Confining Beds as an Oxidant in Microbial Co-2 Production. *J Hydrol* **127**:85-108.
147. **Brown CJ, Coates JD, Schoonen MAA.** 1999. Localized sulfate-reducing zones in a coastal plain aquifer. *Ground Water* **37**:505-516.
148. **Goevert D, Conrad R.** 2010. Stable carbon isotope fractionation by acetotrophic sulfur-reducing bacteria. *Fems Microbiol Ecol* **71**:218-225.
149. **Thauer RK, Postgate JR.** 1982. Dissimilatory Sulfate Reduction with Acetate as Electron-Donor. *Philos T Roy Soc B* **298**:467-&.
150. **Fenchel TM, Jørgensen BB.** 1977. Detritus Food Chains of Aquatic Ecosystems: The Role of Bacteria, p. 1-58. *In* Alexander M (ed.), *Advances in Microbial Ecology*, vol. 1. Springer US.
151. **Widdel F, Pfennig N.** 1981. Studies on dissimilatory sulfate-reducing bacteria that decompose fatty acids. *Arch. Microbiol.* **129**:395-400.
152. **Thauer RK.** 1988. Citric-acid cycle, 50 years on. *European Journal of Biochemistry* **176**:497-508.
153. **Möller D, Schauder R, Fuchs G, Thauer RK.** 1987. Acetate oxidation to CO<sub>2</sub> via a citric acid cycle involving an ATP Citrate lyase - a mechanism for the synthesis of ATP via substrate level phosphorylation in *Desulfobacter postgatei* growing on acetate and sulfate. *Arch. Microbiol.* **148**:202-207.
154. **Ingvorsen K, Zehnder AJ, Jørgensen BB.** 1984. Kinetics of sulfate and acetate uptake by *Desulfobacter postgatei*. *Appl Environ Microbiol* **47**:403-408.
155. **Pires RH, Venceslau SS, Morais F, Teixeira M, Xavier AV, Pereira IAC.** 2006. Characterization of the *Desulfovibrio desulfuricans* ATCC 27774 DsrMKJOP complex - A membrane-bound redox complex involved in the sulfate respiratory pathway. *Biochemistry* **45**:249-262.
156. **Meyer B, Kuehl J, Deutschbauer AM, Price MN, Arkin AP, Stahl DA.** 2013. Variation among *Desulfovibrio* Species in Electron Transfer Systems Used for Syntrophic Growth. *J Bacteriol* **195**:990-1004.
157. **Venceslau SS, Cort JR, Baker ES, Chu RK, Robinson EW, Dahl C, Saraiva LM, Pereira IAC.** 2013. Redox states of *Desulfovibrio vulgaris* DsrC, a key protein in dissimilatory sulfite reduction. *Biochem Bioph Res Co* **441**:732-736.
158. **Keller KL, Bender KS, Wall JD.** 2009. Development of a Markerless Genetic Exchange System for *Desulfovibrio vulgaris* Hildenborough and Its Use in Generating a Strain with Increased Transformation Efficiency. *Appl Environ Microbiol* **75**:7682-7691.

159. **Meyer B, Kuehl JV, Price MN, Ray J, Deutschbauer AM, Arkin AP, Stahl DA.** 2014. The energy-conserving electron transfer system used by *Desulfovibrio alaskensis* strain G20 during pyruvate fermentation involves reduction of endogenously formed fumarate and cytoplasmic and membrane-bound complexes, Hdr-Flox and Rnf. *Environmental Microbiology*:n/a-n/a.
160. **Oliveira TF, Vonnheim C, Matias PM, Venceslau SS, Pereira IAC, Archer M.** 2008. The Crystal Structure of *Desulfovibrio vulgaris* Dissimilatory Sulfite Reductase Bound to DsrC Provides Novel Insights into the Mechanism of Sulfate Respiration. *J. Biol. Chem.* **283**:34141-34149.
161. **Venceslau SS, Lino RR, Pereira IAC.** 2010. The Qrc Membrane Complex, Related to the Alternative Complex III, Is a Menaquinone Reductase Involved in Sulfate Respiration. *J. Biol. Chem.* **285**:22774-22783.
162. **Keller KL, Wall JD.** 2011. Genetics and molecular biology of the electron flow for sulfate respiration in *Desulfovibrio*. *Front Microbiol* **2**.
163. **Pereira IAC, Ramos AR, Grein F, Marques MC, da Silva SM, Venceslau SS.** 2011. A comparative genomic analysis of energy metabolism in sulfate reducing bacteria and archaea. *Front Microbiol* **2**.
164. **Ramos AR, Keller KL, Wall JD, Pereira IAC.** 2012. The membrane QmoABC complex interacts directly with the dissimilatory adenosine 5'-phosphosulfate reductase sulfate reducing bacteria. *Front Microbiol* **3**.
165. **Venceslau SS, Stockdreher Y, Dahl C, Pereira IAC.** 2014. The “bacterial heterodisulfide” DsrC is a key protein in dissimilatory sulfur metabolism. *Biochimica et Biophysica Acta (BBA) - Bioenergetics*.
166. **Grein F, Ramos AR, Venceslau SS, Pereira IAC.** 2013. Unifying concepts in anaerobic respiration: Insights from dissimilatory sulfur metabolism. *Biochimica Et Biophysica Acta-Bioenergetics* **1827**:145-160.
167. **Sun J, Sayyar B, Butler JE, Pharkya P, Fahland TR, Famili I, Schilling CH, Lovley DR, Mahadevan R.** 2009. Genome-scale constraint-based modeling of *Geobacter metallireducens*. *Bmc Syst Biol* **3**.
168. **Sun J, Haveman SA, Bui O, Fahland TR, Lovley DR.** 2010. Constraint-based modeling analysis of the metabolism of two *Pelobacter* species. *Bmc Syst Biol* **4**.
169. **Risso C, Sun J, Zhuang K, Mahadevan R, Deboy R, Ismail W, Shrivastava S, Huot H, Kothari S, Daugherty S, Bui O, Schilling CH, Lovley DR, Methe BA.** 2009. Genome-scale comparison and constraint-based metabolic reconstruction of the facultative anaerobic Fe(III)-reducer *Rhodoferrax ferrireducens*. *Bmc Genomics* **10**.
170. **Zhuang K, Izallalen M, Mouser P, Richter H, Risso C, Mahadevan R, Lovley DR.** 2011. Genome-scale dynamic modeling of the competition between *Rhodoferrax* and *Geobacter* in anoxic subsurface environments. *Isme Journal* **5**:305-316.
171. **Widdel F, Pfennig N.** 1982. Studies on dissimilatory sulfate-reducing bacteria that decompose fatty acids II. Incomplete oxidation of propionate by *Desulfobulbus propionicus* gen. nov., sp. nov. *Arch. Microbiol.* **131**:360-365.
172. **DSMZ** 2014, posting date. List of growth media used at DSMZ. [Online.]

173. **Brown RE, Jarvis KL, Hyland KJ.** 1989. Protein measurement using bicinchoninic acid: elimination of interfering substances. *Analytical Biochemistry* **180**:136-139.
174. **Lovley DR, Phillips EJP.** 1994. Novel Processes for Anaerobic Sulfate Production from Elemental Sulfur by Sulfate-Reducing Bacteria. *Appl Environ Microbiol* **60**:2394-2399.
175. **Esteve-Nunez A, Rothermich M, Sharma M, Lovley D.** 2005. Growth of *Geobacter sulfurreducens* under nutrient-limiting conditions in continuous culture. *Environmental Microbiology* **7**:641-648.
176. **Cordruwisch R.** 1985. A Quick Method for the Determination of Dissolved and Precipitated Sulfides in Cultures of Sulfate-Reducing Bacteria. *J Microbiol Meth* **4**:33-36.
177. **Galushko AS, Schink B.** 2000. Oxidation of acetate through reactions of the citric acid cycle by *Geobacter sulfurreducens* in pure culture and in syntrophic coculture. *Arch. Microbiol.* **174**:314-321.
178. **Tempest DW, Neijssel OM.** 1984. The Status of  $Y_{atp}$  and Maintenance Energy as Biologically Interpretable Phenomena. *Annu Rev Microbiol* **38**:459-486.
179. **Hazeu W, Bijleveld W, Grotenhuis JTC, Kakes E, Kuenen JG.** 1986. Kinetics and energetics of reduced sulfur oxidation by chemostat cultures of *Thiobacillus ferrooxidans*. *Antonie van Leeuwenhoek* **52**:507-518.
180. **Han C, Chain P.** 2006. Finishing Repetitive Regions Automatically with Dupfinisher, p. 142-147.
181. **Badger JH, Olsen GJ.** 1999. CRITICA: Coding region identification tool invoking comparative analysis. *Mol Biol Evol* **16**:512-524.
182. **Delcher AL, Harmon D, Kasif S, White O, Salzberg SL.** 1999. Improved microbial gene identification with GLIMMER. *Nucleic Acids Res* **27**:4636-4641.
183. **Lowe TM, Eddy SR.** 1997. tRNAscan-SE: a program for improved detection of transfer RNA genes in genomic sequence. *Nucleic Acids Res* **25**:955-964.
184. **Markowitz VM, Mavromatis K, Ivanova NN, Chen IMA, Chu K, Kyrpides NC.** 2009. IMG ER: a system for microbial genome annotation expert review and curation. *Bioinformatics* **25**:2271-2278.
185. **Kumar VS, Dasika MS, Maranas CD.** 2007. Optimization based automated curation of metabolic reconstructions. *Bmc Bioinformatics* **8**.
186. **Izard J, Limberger RJ.** 2003. Rapid screening method for quantitation of bacterial cell lipids from whole cells. *J Microbiol Meth* **55**:411-418.
187. **Ashwell G.** 1957. Colorimetric Analysis of Sugars. *Method Enzymol* **3**:73-105.
188. **Islam MA, Edwards EA, Mahadevan R.** 2010. Characterizing the Metabolism of *Dehalococcoides* with a Constraint-Based Model. *Plos Comput Biol* **6**.
189. **Feist AM, Henry CS, Reed JL, Krummenacker M, Joyce AR, Karp PD, Broadbelt LJ, Hatzimanikatis V, Palsson BO.** 2007. A genome-scale metabolic reconstruction for *Escherichia coli* K-12 MG1655 that accounts for 1260 ORFs and thermodynamic information. *Mol Syst Biol* **3**.
190. **Methé BA, Webster J, Nevin K, Butler J, Lovley DR.** 2005. DNA Microarray Analysis of Nitrogen Fixation and Fe(III) Reduction in *Geobacter sulfurreducens*. *Appl Environ Microbiol* **71**:2530-2538.

191. **Shrestha PM, Kube M, Reinhardt R, Liesack W.** 2009. Transcriptional activity of paddy soil bacterial communities. *Environ Microbiol* **11**:960-970.
192. **Schmieder R, Edwards R.** 2011. Quality control and preprocessing of metagenomic datasets. *Bioinformatics* **27**:863-864.
193. **Mortazavi A, Williams BA, Mccue K, Schaeffer L, Wold B.** 2008. Mapping and quantifying mammalian transcriptomes by rna-seq. *Nat Meth.* 8 p. *Nature Methods*:8.
194. **Klevebring D, Bjursell M, Emanuelsson O, Lundeberg J.** 2010. In-depth transcriptome analysis reveals novel TARs and prevalent antisense transcription in human cell lines. *Plos One* **5**:e9762.
195. **Buckel W, Thauer RK.** 2013. Energy conservation via electron bifurcating ferredoxin reduction and proton/Na<sup>+</sup> translocating ferredoxin oxidation. *Biochimica Et Biophysica Acta-Bioenergetics* **1827**:94-113.
196. **Thauer RK, Jungermann K, Decker K.** 1977. Energy conservation in chemotrophic anaerobic bacteriad. *Bacteriological reviews* **41**:100-180.
197. **Rabus R, Hansen T, Widdel F.** 2006. Dissimilatory Sulfate- and Sulfur-Reducing Prokaryotes, p. 659-768. *In* Dworkin M, Falkow S, Rosenberg E, Schleifer K-H, Stackebrandt E (ed.), *The Prokaryotes*. Springer New York.
198. **Möller-Zinkhan D, Thauer RK.** 1988. Membrane-bound NADPH dehydrogenase and ferredoxin:NADP oxidoreductase activity involved in electron transport during acetate oxidation to CO<sub>2</sub> in *Desulfobacter postgatei*. *Arch. Microbiol.* **150**:145-154.
199. **Postgate J.** 1995. Breathless niches. *Nature* **377**:26-26.
200. **Pereira MM, Refojo PN, Hreggvidsson GO, Hjorleifsdottir S, Teixeira M.** 2007. The alternative complex III from *Rhodothermus marinus* – A prototype of a new family of quinol:electron acceptor oxidoreductases. *FEBS Letters* **581**:4831-4835.
201. **Gao XL, Xin YY, Blankenship RE.** 2009. Enzymatic activity of the alternative complex III as a menaquinol: auracyanin oxidoreductase in the electron transfer chain of *Chloroflexus aurantiacus*. *FEBS Letters* **583**:3275-3279.
202. **Barton L, Hamilton WA.** 2007. Sulphate-reducing bacteria : environmental and engineered systems. Cambridge University Press, Cambridge ; New York.
203. **Odom JM, Peck HD.** 1981. Hydrogen cycling as a general mechanism for energy coupling in the sulfate-reducing bacteria, *Desulfovibrio sp.* *Fems Microbiol Lett* **12**:47-50.
204. **Rodrigues R, Valente FMA, Pereira IAC, Oliveira S, Rodrigues-Pousada C.** 2003. A novel membrane-bound Ech [NiFe] hydrogenase in *Desulfovibrio gigas*. *Biochem Bioph Res Co* **306**:366-375.
205. **Caffrey SA, Park HS, Voordouw JK, He Z, Zhou J, Voordouw G.** 2007. Function of periplasmic hydrogenases in the sulfate-reducing bacterium *Desulfovibrio vulgaris* Hildenborough. *J Bacteriol* **189**:6159-6167.
206. **Spring S, Visser M, Lu M, Copeland A, Lapidus A, Lucas S, Cheng JF, Han C, Tapia R, Goodwin LA, Pitluck S, Ivanova N, Land M, Hauser L, Larimer F, Rohde M, Goker M, Detter JC, Kyrpides NC, Woyke T, Schaap PJ, Plugge CM, Muyzer G, Kuever J, Pereira IAC, Parshina SN, Bernier-Latmani R, Stams AJM, Klenk HP.** 2012. Complete genome sequence of the

- sulfate-reducing firmicute *Desulfotomaculum ruminis* type strain (DLT). *Stand Genomic Sci* **7**:304-319.
207. **Welte C, Kratzer C, Deppenmeier U.** 2010. Involvement of Ech hydrogenase in energy conservation of *Methanosarcina mazei*. *Febs J* **277**:3396-3403.
  208. **Coppi MV.** 2005. The hydrogenases of *Geobacter sulfurreducens*: a comparative genomic perspective. *Microbiology* **151**:1239-1254.
  209. **Vignais PM, Billoud B.** 2007. Occurrence, classification, and biological function of hydrogenases: An overview. *Chem Rev* **107**:4206-4272.
  210. **Price ND, Schellenberger J, Palsson BO.** 2004. Uniform sampling of steady-state flux spaces: Means to design experiments and to interpret enzymopathies. *Biophys J* **87**:2172-2186.
  211. **Strittmatter AW, Liesegang H, Rabus R, Decker I, Amann J, Andres S, Henne A, Fricke WF, Martinez-Arias R, Bartels D, Goesmann A, Krause L, Puhler A, Klenk HP, Richter M, Schuler M, Glockner FO, Meyerdierks A, Gottschalk G, Amann R.** 2009. Genome sequence of *Desulfobacterium autotrophicum* HRM2, a marine sulfate reducer oxidizing organic carbon completely to carbon dioxide. *Environmental Microbiology* **11**:1038-1055.
  212. **McInerney MJ, Rohlin L, Mouttaki H, Kim U, Krupp RS, Rios-Hernandez L, Sieber J, Struchtemeyer CG, Bhattacharyya A, Campbell JW, Gunsalus RP.** 2007. The genome of *Syntrophus aciditrophicus*: life at the thermodynamic limit of microbial growth. *Proc Natl Acad Sci U S A* **104**:7600-7605.
  213. **Muller V, Imkamp F, Biegel E, Schmidt S, Dilling S.** 2008. Discovery of a Ferredoxin : NAD(+)-Oxidoreductase (Rnf) in *Acetobacterium woodii* - A novel potential coupling site in acetogens. *Ann Ny Acad Sci* **1125**:137-146.
  214. **Seedorf H, Fricke WF, Veith B, Bruggemann H, Liesegang H, Strittmatter A, Miethke M, Buckel W, Hinderberger J, Li FL, Hagemeyer C, Thauer RK, Gottschalk G.** 2008. The genome of *Clostridium kluyveri*, a strict anaerobe with unique metabolic features. *Proceedings of the National Academy of Sciences of the United States of America* **105**:2128-2133.
  215. **Kopke M, Held C, Hujer S, Liesegang H, Wiezer A, Wollherr A, Ehrenreich A, Liebl W, Gottschalk G, Durre P.** 2010. *Clostridium ljungdahlii* represents a microbial production platform based on syngas. *Proceedings of the National Academy of Sciences of the United States of America* **107**:13087-13092.
  216. **Biegel E, Schmidt S, Gonzalez JM, Muller V.** 2011. Biochemistry, evolution and physiological function of the Rnf complex, a novel ion-motive electron transport complex in prokaryotes. *Cell Mol Life Sci* **68**:613-634.
  217. **Poehlein A, Daniel R, Schink B, Simeonova DD.** 2013. Life based on phosphite: a genome-guided analysis of *Desulfotignum phosphitoxidans*. *Bmc Genomics* **14**.
  218. **Feist AM, Palsson BO.** 2010. The biomass objective function. *Current opinion in microbiology* **13**:344-349.
  219. **Thiele I, Palsson BO.** 2010. A protocol for generating a high-quality genome-scale metabolic reconstruction. *Nat. Protocols* **5**:93-121.
  220. **Hyduke D, Schellenberger J, Que R, Fleming R, Thiele I, Orth J, Feist A, Zielinski D, Bordbar A, Lewis N, Rahmanian S, Kang J, Palsson B.** 2011. COBRA Toolbox 2.0.



221. **Pirt SJ.** 1965. The maintenance energy of bacteria in growing cultures. *Proc R Soc Lond B Biol Sci* **163**:224-231.
222. **Schauder R, Widdel F, Fuchs G.** 1987. Carbon assimilation pathways in sulfate-reducing bacteria II. Enzymes of a reductive citric acid cycle in the autotrophic *Desulfobacter hydrogenophilus*. *Arch. Microbiol.* **148**:218-225.
223. **Hoehler TM, Jørgensen BB.** 2013. Microbial life under extreme energy limitation. *Nat Rev Micro* **11**:83-94.
224. **van Bodegom P.** 2007. Microbial maintenance: a critical review on its quantification. *Microb Ecol* **53**:513-523.
225. **Davidson MM, Bisher ME, Pratt LM, Fong J, Southam G, Pfiffner SM, Reches Z, Onstott TC.** 2009. Sulfur Isotope Enrichment during Maintenance Metabolism in the Thermophilic Sulfate-Reducing Bacterium *Desulfotomaculum putei*. *Appl Environ Microbiol* **75**:5621-5630.
226. **Schonheit P, Kristjansson JK, Thauer RK.** 1982. Kinetic mechanism for the ability of sulfate reducers to outcompete methanogens for acetate. *Arch. Microbiol.* **132**:285-288.
227. **Stefanie JWH, Elferink O, Visser A, Hulshoff Pol LW, Stams AJM.** 1994. Sulfate reduction in methanogenic bioreactors. *FEMS Microbiology Reviews* **15**:119-136.
228. **Kristjansson JK, Schönheit P.** 1983. Why do sulfate-reducing bacteria outcompete methanogenic bacteria for substrates? *Oecologia* **60**:264-266.
229. **Jin Q.** 2012. Energy conservation of anaerobic respiration. *American Journal of Science* **312**:573-628.
230. **Edwards JS, Ramakrishna R, Palsson BO.** 2002. Characterizing the metabolic phenotype: a phenotype phase plane analysis. *Biotechnol Bioeng* **77**:27-36.
231. **Edwards JS, Ibarra RU, Palsson BO.** 2001. *In silico* predictions of *Escherichia coli* metabolic capabilities are consistent with experimental data. *Nat Biotechnol* **19**:125-130.
232. **Thiele I, Price ND, Vo TD, Palsson BO.** 2005. Candidate metabolic network states in human mitochondria. *J. Biol. Chem.* **280**:11683-11695.
233. **Zomorodi AR, Suthers PF, Ranganathan S, Maranas CD.** 2012. Mathematical optimization applications in metabolic networks. *Metab Eng* **14**:672-686.
234. **Yoon K-S, Ishii M, Kodama T, Igarashi Y.** 1997. Carboxylation Reactions of Pyruvate: Ferredoxin Oxidoreductase and 2-Oxoglutarate: Ferredoxin Oxidoreductase from *Hydrogenobacter thermophilus* TK-6. *Bioscience, Biotechnology, and Biochemistry* **61**:510-513.
235. **Villanueva L, Haveman SA, Summers ZM, Lovley DR.** 2008. Quantification of *Desulfovibrio vulgaris* dissimilatory sulfite reductase gene expression during electron donor- and electron acceptor-limited growth. *Appl Environ Microbiol* **74**:5850-5853.
236. **Keller KL, Rapp-Giles BJ, Semkiw ES, Porat I, Brown SD, Wall JD.** 2014. New Model for Electron Flow for Sulfate Reduction in *Desulfovibrio alaskensis* G20. *Appl Environ Microbiol* **80**:855-868.

237. **Meyer B, Kuehl JV, Deutschbauer AM, Arkin AP, Stahl DA.** 2013. Flexibility of Syntrophic Enzyme Systems in *Desulfovibrio* Species Ensures Their Adaptation Capability to Environmental Changes. *J Bacteriol* **195**:4900-4914.
238. **Carbonero F, Oakley BB, Purdy KJ.** 2014. Metabolic Flexibility as a Major Predictor of Spatial Distribution in Microbial Communities. *Plos One* **9**.
239. **Krogh A, Larsson B, von Heijne G, Sonnhammer ELL.** 2001. Predicting transmembrane protein topology with a hidden Markov model: Application to complete genomes. *J Mol Biol* **305**:567-580.
240. **Price M, Ray J, Wetmore KM, Kuehl JV, Bauer S, Deutschbauer AM, Arkin AP.** 2014. The genetic basis of energy conservation in the sulfate-reducing bacterium *Desulfovibrio alaskensis* G20.
241. **Ingvorsen K, Zehnder AJB, Jorgensen BB.** 1984. Kinetics of Sulfate and Acetate Uptake by *Desulfobacter postgatei*. *Appl Environ Microb* **47**:403-408.
242. **Widdel F, Pfennig N.** 1981. Studies on Dissimilatory Sulfate-Reducing Bacteria That Decompose Fatty-Acids .1. Isolation of New Sulfate-Reducing Bacteria Enriched with Acetate from Saline Environments - Description of *Desulfobacter postgatei* gen-nov, sp-nov. *Arch. Microbiol.* **129**:395-400.
243. **Wolfe AJ.** 2005. The acetate switch. *Microbiol Mol Biol R* **69**:12-+.
244. **Stahlmann J, Warthmann R, Cypionka H.** 1991. Na<sup>+</sup>-Dependent Accumulation of Sulfate and Thiosulfate in Marine Sulfate-Reducing Bacteria. *Arch. Microbiol.* **155**:554-558.
245. **Brandis-Heep A, Gebhardt NA, Thauer RK, Widdel F, Pfennig N.** 1983. Anaerobic Acetate Oxidation to CO<sub>2</sub> by *Desulfobacter postgatei* .1. Demonstration of All Enzymes Required for the Operation of the Citric-Acid Cycle. *Arch. Microbiol.* **136**:222-229.
246. **Möller-Zinkhan D, Thauer RK.** 1988. Membrane-bound NADPH dehydrogenase- and ferredoxin: NADP oxidoreductase activity involved in electron transport during acetate oxidation to CO<sub>2</sub> in *Desulfobacter postgatei*. *Arch. Microbiol.* **150**:145-154.
247. **Ivanovsky RN, Sintsov NV, Kondratieva EN.** 1980. ATP-linked citrate lyase activity in the green sulfur bacterium *Chlorobium limicola* forma *thiosulfatophilum*. *Arch. Microbiol.* **128**:239-241.
248. **Thauer RK, Moller-Zinkhan D, Spormann AM.** 1989. Biochemistry of acetate catabolism in anaerobic chemotrophic bacteria. *Annu Rev Microbiol* **43**:43-67.
249. **Atomi H.** 2002. Microbial enzymes involved in carbon dioxide fixation. *Journal of Bioscience and Bioengineering* **94**:497-505.
250. **Rabus R, Hansen TA, Widdel F.** 2006. Dissimilatory Sulfate- and Sulfur-Reducing Prokaryotes. *Prokaryotes: A Handbook on the Biology of Bacteria*, Vol 2, Third Edition:659-768.
251. **Costa C, Moura JJG, Moura I, Liu MY, Peck HD, Legall J, Wang YN, Huynh BH.** 1990. Hexaheme Nitrite Reductase from *Desulfovibrio desulfuricans*. Mössbauer and EPR Characterization of the Heme Groups. *J. Biol. Chem.* **265**:14382-14388.
252. **Mahadevan R, Lovley DR.** 2008. The degree of redundancy in metabolic genes is linked to mode of metabolism. *Biophys J* **94**:1216-1220.

253. **Segura D, Mahadevan R, Juárez K, Lovley DR.** 2008. Computational and Experimental Analysis of Redundancy in the Central Metabolism of *Geobacter sulfurreducens*. *Plos Comput Biol* **4**:e36.
254. **Yang TH, Coppi M, Lovley D, Sun J.** 2010. Metabolic response of *Geobacter sulfurreducens* towards electron donor/acceptor variation. *Microbial Cell Factories* **9**:90.
255. **Sousa FL, Thiergart T, Landan G, Nelson-Sathi S, Pereira IA, Allen JF, Lane N, Martin WF.** 2013. Early bioenergetic evolution. *Philosophical transactions of the Royal Society of London. Series B, Biological sciences* **368**:20130088.
256. **Ramos AR, Keller KL, Wall JD, Pereira IAC.** 2012. The membrane QmoABC complex interacts directly with the dissimilatory adenosine 5'-phosphosulfate reductase in sulfate reducing bacteria. *Front Microbiol* **3**.
257. **Pires RH, Lourenco AI, Morais F, Teixeira M, Xavier AV, Saraiva LM, Pereira IAC.** 2003. A novel membrane-bound respiratory complex from *Desulfovibrio desulfuricans* ATCC 27774. *Biochimica Et Biophysica Acta-Bioenergetics* **1605**:67-82.
258. **Krumholz LR, Wang L, Beck DAC, Wang T, Hackett M, Mooney B, Juba TR, McInerney MJ, Meyer B, Wall JD, Stahl DA.** 2013. Membrane protein complex of APS reductase and Qmo is present in *Desulfovibrio vulgaris* and *Desulfovibrio alaskensis*. *Microbiology* **159**:2162-2168.
259. **Grein F, Pereira IAC, Dahl C.** 2010. Biochemical Characterization of Individual Components of the *Allochromatium vinosum* DsrMKJOP Transmembrane Complex Aids Understanding of Complex Function *In Vivo*. *J Bacteriol* **192**:6369-6377.
260. **Klenk HP, Clayton RA, Tomb JF, White O, Nelson KE, Ketchum KA, Dodson RJ, Gwinn M, Hickey EK, Peterson JD, Richardson DL, Kerlavage AR, Graham DE, Kyrpides NC, Fleischmann RD, Quackenbush J, Lee NH, Sutton GG, Gill S, Kirkness EF, Dougherty BA, McKenney K, Adams MD, Loftus B, Peterson S, Reich CI, McNeil LK, Badger JH, Glodek A, Zhou LX, Overbeek R, Gocayne JD, Weidman JF, McDonald L, Utterback T, Cotton MD, Spriggs T, Artiach P, Kaine BP, Sykes SM, Sadow PW, D'Andrea KP, Bowman C, Fujii C, Garland SA, Mason TM, Olsen GJ, Fraser CM, Smith HO, Woese CR, Venter JC.** 1998. The complete genome sequence of the hyperthermophilic, sulphate-reducing archaeon *Archaeoglobus fulgidus*. *Nature* **394**:101-101.
261. **Junier P, Junier T, Podell S, Sims DR, Detter JC, Lykidis A, Han CS, Wigginton NS, Gaasterland T, Bernier-Latmani R.** 2010. The genome of the Gram positive metal- and sulfate-reducing bacterium *Desulfotomaculum reducens* strain MI-1. *Environmental Microbiology* **12**:2738-2754.
262. **Heidelberg JF, Seshadri R, Haveman SA, Hemme CL, Paulsen IT, Kolonay JF, Eisen JA, Ward N, Methe B, Brinkac LM, Daugherty SC, Deboy RT, Dodson RJ, Durkin AS, Madupu R, Nelson WC, Sullivan SA, Fouts D, Haft DH, Selengut J, Peterson JD, Davidsen TM, Zafar N, Zhou LW, Radune D, Dimitrov G, Hance M, Tran K, Khouri H, Gill J, Utterback TR, Feldblyum TV, Wall JD, Voordouw G, Fraser CM.** 2004. The genome sequence of the

- anaerobic, sulfate-reducing bacterium *Desulfovibrio vulgaris* Hildenborough. Nature Biotechnology **22**:554-559.
263. **Brown SD, Gilmour CC, Kucken AM, Wall JD, Elias DA, Brandt CC, Podar M, Chertkov O, Held B, Bruce DC, Detter JC, Tapia R, Han CS, Goodwin LA, Cheng JF, Pitluck S, Woyke T, Mikhailova N, Ivanova NN, Han J, Lucas S, Lapidus AL, Land ML, Hauser LJ, Palumbo AV.** 2011. Genome Sequence of the Mercury-Methylating Strain *Desulfovibrio desulfuricans* ND132. J Bacteriol **193**:2078-2079.
264. **Wang S, Huang H, Moll J, Thauer RK.** 2010. NADP<sup>+</sup> Reduction with Reduced Ferredoxin and NADP<sup>+</sup> Reduction with NADH Are Coupled via an Electron-Bifurcating Enzyme Complex in *Clostridium kluyveri*. J Bacteriol **192**:5115-5123.
265. **Andrews SC, Berks BC, McClay J, Ambler A, Quail MA, Golby P, Guest JR.** 1997. A 12-cistron *Escherichia coli* operon (hyf) encoding a putative proton-translocating formate hydrogenlyase system. Microbiology **143**:3633-3647.
266. **Kunkel A, Vorholt JA, Thauer RK, Hedderich R.** 1998. An *Escherichia coli* hydrogenase-3-type hydrogenase in methanogenic archaea. European Journal of Biochemistry **252**:467-476.
267. **Sapra R, Verhagen MFJM, Adams MWW.** 2000. Purification and characterization of a membrane-bound hydrogenase from the hyperthermophilic archaeon *Pyrococcus furiosus*. J Bacteriol **182**:3423-3428.
268. **Clark ME, He ZL, Redding AM, Joachimiak MP, Keasling JD, Zhou JZZ, Arkin AP, Mukhopadhyay A, Fields MW.** 2012. Transcriptomic and proteomic analyses of *Desulfovibrio vulgaris* biofilms: Carbon and energy flow contribute to the distinct biofilm growth state. BMC Genomics **13**.
269. **Yu NY, Wagner JR, Laird MR, Melli G, Rey S, Lo R, Dao P, Sahinalp SC, Ester M, Foster LJ, Brinkman FSL.** 2010. PSORTb 3.0: improved protein subcellular localization prediction with refined localization subcategories and predictive capabilities for all prokaryotes. Bioinformatics **26**:1608-1615.
270. **Barton L.** 1995. Sulfate-reducing bacteria. Plenum Press, New York.
271. **Dar SA, Kleerebezem R, Stams AJM, Kuenen JG, Muyzer G.** 2008. Competition and coexistence of sulfate-reducing bacteria, acetogens and methanogens in a lab-scale anaerobic bioreactor as affected by changing substrate to sulfate ratio. Appl Microbiol Biot **78**:1045-1055.
272. **Kobayashi K, Hasegawa H, Takagi M, Ishimoto M.** 1982. Proton translocation associated with sulfite reduction in a sulfate-reducing bacterium, *Desulfovibrio vulgaris*. Febs Letters **142**:235-237.
273. **Neidhardt FC, Ingraham JL, Schaechter M.** 1990. Physiology of the bacterial cell: a molecular approach. Sinauer Associates, Inc, Sunderland, Mass.
274. **Orth JD, Conrad TM, Na J, Lerman JA, Nam H, Feist AM, Palsson BO.** 2011. A comprehensive genome-scale reconstruction of *Escherichia coli* metabolism--2011. Mol Syst Biol **7**:65.